Supplementary Information for:

A Genome-Wide Investigation into Parent-of-Origin Effects in Autism Spectrum Disorder Identifies Previously Associated Genes including *SHANK3*.

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Materials and Methods

Statistical Model

Estimation of Maternal, Imprinting and interaction effects using Multinomial Modelling (EMIM) [1] directly maximises the multinomial likelihood to detect parent-of-origin effects. EMIM has many advantages over other statistical methods (such as LRT [2], PO-LRT [3], CPG [4] and CEPG [4]) for detecting parent-of-origin effects as EMIM has consistent type I error rates, in general offers the strongest power and is flexible in study and model design [5]. The theoretical frequencies for the multinomial model are shown in Table S1, where column 5 gives the parameters that are

Table S1: Theoretical Frequencies for Family Trios

No. of Variant Alleles (MPC[a])	Parental Origin (Mat and/or Pat)	Mating Type	Theoretical Frequency[b]	EMIM Parameters[c]
222	Mat & Pat	1	$S_2R_2I_MI_P\alpha_{22}\mu_1$	$(S_1)^2(R_1^*)^2I_M^*\mu_1$
212	Mat & Pat	2	$S_2R_2I_MI_P\mu_2$	$(S_1)^2(R_1^*)^2I_M^*\mu_2$
122	Mat & Pat	2	$S_1R_2I_MI_P\alpha_{12}\mu_2$	$S_1(R_1^*)^2I_M^*\mu_2$
211	Mat	2	$S_2R_1I_M\alpha_{21}\mu_2$	$(S_1)^2R_1^*I_M^*\mu_2$
121	Pat	2	$S_1R_1I_P\alpha_{12}\mu_2$	$S_1R_1^*\alpha_{11}\mu_2$
201	Mat	3	$S_2R_1I_M\mu_3$	$(S_1)^2R_1^*I_M^*\mu_3$
021	Pat	3	$R_1I_P\mu_3$	$R_1^*\mu_3$
112	Mat & Pat	4	$S_1R_2I_MI_P\alpha_{11}\mu_4$	$S_1(R_1^*)^2I_M^*\alpha_{12}^*\mu_4$
111	Mat or Pat	4	$S_1R_1(I_M+I_P)\alpha_{11}\mu_4$	$S_1R_1^*(I_M^*+1)\alpha_{11}\mu_4$
110		4	$S_1\alpha_{11}\mu_4$	$S_1\mu_4$
101	Mat	5	$S_1R_1I_M\mu_5$	$S_1R_1^*I_M^*\alpha_{11}\mu_5$
011	Pat	5	$R_1I_P\mu_5$	$R_1^*\mu_5$
100		5	$S_1\mu_5$	$S_1\mu_5$
010		5	μ_5	μ_5
000		6	μ_6	μ_6

[a] M,P and C are the number of copies of the allele the mother, father and offspring possess, respectively.

[b] R_k, S_j and α_{jk}, for j,k $\in \{1,2\}$, denote the relative risk associated with $j = M$ and $k = C$ copies. I_M and I_P denote the relative risk associated with the allele originating from the mother and the father respectively, compared to the risk associated with the allele not being inherited. μ_i for i $\in \{1,..,6\}$ are the relative frequencies for the 6 different parental-mating types shown in Column 3.

[c] These are the parameters that can be estimated in EMIM as defined here with $R_1^* = R_1I_P$, $R_2^* = R_2(I_P)^2$, $I_M^* = I_M/I_P$ and assuming a multiplicative model leads to $(S_1)^2 = S_2$ and $(R_1)^2 = R_2 \Longrightarrow (R_1^*)^2 = (R_2^*)^2$.

estimated in the model for this analysis. Mother/offspring interactions were not included in the model due to power issues, although we did investigate these interactions when an offspring genetic effect and maternal genetic effect were identified. In this scenario, the model is run again in EMIM at only this SNP but this time including interactions in the model and utilising the Likelihood Ratio Test (LRT) to compare the model with interactions to the model without interactions. The model in EMIM assumes a genetic multiplicative model, shown in column 5, Table S1. Assuming a multiplicative model can help increase power under certain genetic models (such as a true dominant model) and is robust even when the model is misspecified [6]. One exception is when the true model is a recessive model, however there is little power to detect a recessive variant even when correctly specified [6]. Note: we assume parental mating symmetry (shown in column 3, Table S1) in the population (when the proportion of matings with mothers of genotype M = m and fathers of genotype P = p is the same as the proportion of matings with mothers of genotype M = p and fathers of genotype P = m for the population) in order to investigate maternal genetic effects.

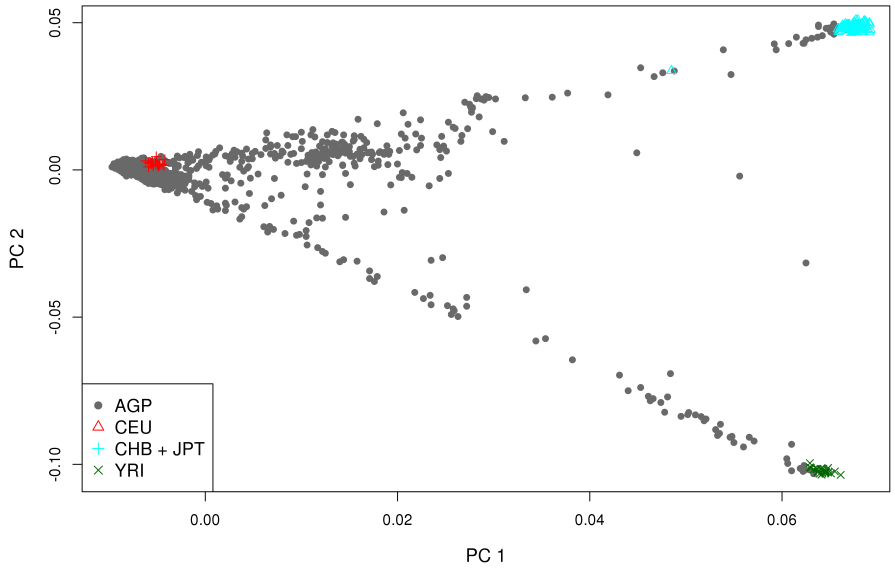
Quality Control Procedures

Quality Control (QC) procedures involve two main steps, QC of individuals and QC of SNPs. We conducted the QC procedures using PLINK [7] and R [8]. We carried out our QC procedures on the Strict Autism phenotype separate to the Spectrum Autism phenotype. This was necessary in order to ensure that only the individuals included in the dataset would have an influence on the SNPs that passed our QC criteria.

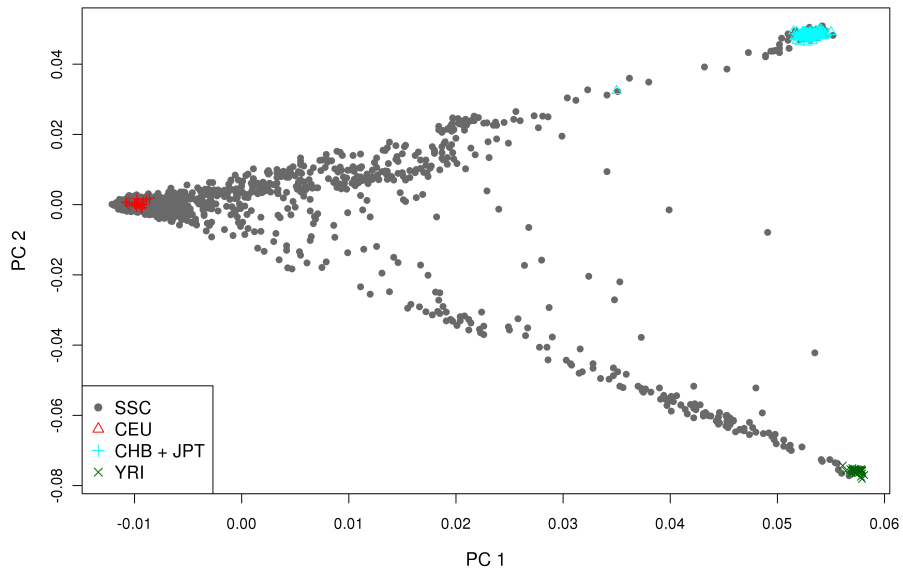
We carried out Principal Component Analyses (PCA) (Eigenstrat, [9]) for both the AGP and SSC data to examine the structure of the populations using only high quality independent SNPs from one affected offspring per family with HapMap data [10] as a reference. From Figure S1, it is evident that the majority of samples from both the AGP and SSC are of European descent. We did

not remove individuals that were not of European descent as we did not assume Hardy-Weinberg equilibrium (HWE) in our model in EMIM, but we did assume parental symmetry and we stratified the data into six mating types in order to make the model robust against population stratification.

For our analyses, we only considered independent trios consisting of one affected offspring



(a) AGP



(b) SSC

Figure S1: Principal Component Analysis for the AGP and SSC data including the Hapmap data (release 23) for reference.

and two genotyped parents. Only considering trios reduces the amount of missing genotype data that needs to be estimated in EMIM, thus potentially increasing power. In the families with more than one affected sibling, we randomly selected a sibling to include and removed all other(s). Filtering of high call rates (>95%) for both the SNPs and the individuals was then carried out. We QC'd the data for any serious deviations from HWE (p-value < 0.00001) because even though we did not assume HWE in our model (we assumed parental symmetry), HWE can also detect genotyping error and non-random mating such as inbreeding. We removed SNPs with MAF $< 5\%$. We investigated individuals and SNPs for Mendelian errors and any errors that were below 0.05% (minor errors) were set to missing. We also removed any extreme deviations of heterozygosity and checked for relatedness between families. We also removed any other SNPs that had a HWE p-value < 0.00001 again in order to make the model more robust to population stratification. At each QC step we removed any families that did not consist of complete trios. See Table S2 and Table S3 for further details on the QC.

Table S2: Quality Control Procedure for AGP datasets

	Strict AGP Data		**Spectrum AGP Data**	
	Families	**SNPs**	**Families**	**SNPs**
Start:	2 931	924 324	2 931	924 324
Autosomal SNPs	2 931	908 421	2 931	908 421
1 affected offspring & 2 parents	1 723	908 421	2 782	908 421
QC Steps:				
Call Rate < 95%	62	70 741	90	70 554
HWE < 0.00001	-	20 744	-	31 811
MAF < 5%	-	81 974	-	77 796
Mendelian Errors > 0.5%	0	0	0	0
Heterozygosity	62	-	88	-
Relatedness	5	-	10	-
HWE < 0.00001	-	37	-	32
Final	1 594	734 925	2 594	728 228

Table S3: Quality Control Procedure for SSC datasets

	Strict SSC Data		Spectrum SSC Data	
	Families	**SNPs**	**Families**	**SNPs**
Start:	2 591	645 885	2 591	645 885
Autosomal SNPs	2 591	626 243	2 591	626 243
1 affected offspring & 2 parents	2 089	626 243	2 586	626 243
QC Steps:				
Call Rate < 95%	0	3 843	0	3 877
HWE < 0.00001	-	55 821	-	62 430
MAF < 5%	-	76 513	-	74 286
Mendelian Errors > 0.5%	1	2 769	1	2 596
Heterozygosity	68	-	108	-
Relatedness	60	-	44	-
HWE < 0.00001	-	91	-	64
Final	1 960	487 216	2 433	483 080

Bayesian Noteworthy Threshold

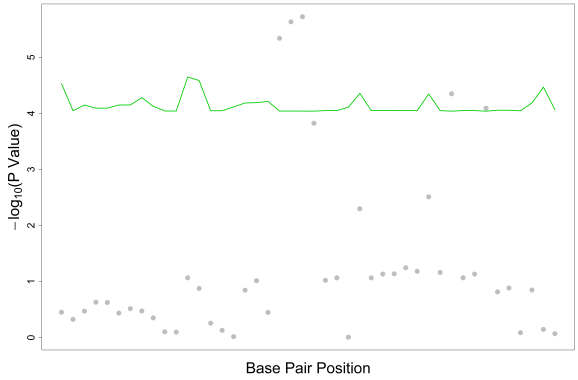
In specifying the parameters for the Bayesian thresholds for R_1 and S_1, we note that the effect sizes in GWAS for a complex disorder are generally expected to be low. For example, the genotype relative risk for a SNP is suggested to be between 1.1 and 2 [11, 12]. The most significant findings in previous GWASs in ASD include a SNP (rs4307059) on chromosome 5 with an odds ratio of 1.19 [13], another SNP (rs10513025) on chromosome 5 with an odds ratio of 0.55 ($1/0.55 = 1.81$) [14] and a SNP (rs4141463) in the gene *MACROD2* on chromosome 20 with an odds ratio of 0.56 ($1/0.56 = 1.79$) [15]. These previous findings all report effect sizes in terms of odds ratios. In comparing odds ratios and relative risks, these effect sizes will be similar when the event of interest is rare, otherwise the odds ratio will overestimate the relative risk. Based on the suggested range of relative risk sizes and odds ratio findings, we chose the prior on the effect size for an association and a maternal genetic effect such that there is a 5% chance that the relative risk will be larger than 2. This results in the prior variance for the log of the relative risk being $W = 0.42^2$ [16].

There is evidence to suggest that there are several hundred to thousands of loci that are likely

to contribute to the complex genetic heterogeneity of ASD [17–19], the majority of which are due to common variation [20]. If we conservatively assume that there are 1 million independent common variants and that 500 of these variants contribute to ASD, then our prior probability that H_0 is true, π_0 = 1 - 500/1,000,000 = 0.9995, leads to a prior odds of H_0 being true of PO = 1,999. We chose $R = 10$, the ratio of cost of type II to type I error. We believe type II errors are 10 times as bad as type I errors, as false negative findings cannot be followed up as noted and discussed by Wakefield [21].

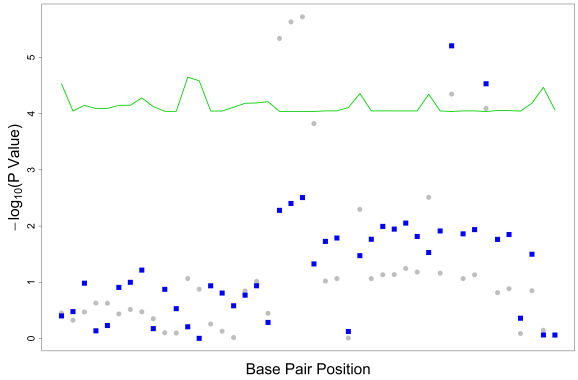
The standard errors in the full model produced by EMIM can be inflated [1] and when the standard error (V_n) increases, Z^2 score increases. Instead of using the standard error of R_1 (offspring genetic effect) and S_1 (maternal genetic effect) for V_n that the full model produces, we used the standard errors from testing for R_1 and S_1 independently (e.g. H_0: $R_1 = 0$ and H_1: $R_1 \neq 0$). Therefore, the standard error for R_1 and S_1 is calculated using $[\text{n} \times \text{MAF} \times (1 - \text{MAF})]^{-\frac{1}{2}}$, where n is the sample size and the MAF is the minor allele frequency calculated using the offsprings' genotypes when calculating the standard error for R_1 and using the mothers' genotypes when calculating the standard error for S_1.

We calculated a Z^2 score threshold for the Wald Z score for R_1 (the association parameter) and then on finding results above this threshold, we investigated further for an imprinting effect using the Wald p-value for I_M (the imprinting parameter). We identified a noteworthy imprinting result when the imprinting Wald p-value is greater than the association threshold also. This process is illustrated in Figure S2, using dummy data. We calculated a Z^2 score threshold for the Wald Z score for S_1 (maternal genetic effect) and a noteworthy maternal genetic effect is identified when S_1 is above this threshold. It is not necessary to have also identified an association at this locus. Figure S3 illustrates how we identified noteworthy maternal genetic effects.



SNP	R_1 Threshold	P-value R_1	P-value I_M
rs48	$1.22\text{x}10^{-4}$	$\mathbf{1.10\text{x}10^{-6}}$	$8.33\text{x}10^{-3}$
rs46	$1.18\text{x}10^{-4}$	$\mathbf{1.85\text{x}10^{-6}}$	$8.78\text{x}10^{-3}$
rs43	$1.09\text{x}10^{-4}$	$\mathbf{3.48\text{x}10^{-6}}$	$9.22\text{x}10^{-3}$
rs88	$1.03\text{x}10^{-4}$	$\mathbf{7.48\text{x}10^{-5}}$	$1.31\text{x}10^{-5}$
rs99	$1.12\text{x}10^{-4}$	$\mathbf{9.81\text{x}10^{-5}}$	$7.18\text{x}10^{-5}$
rs54	$9.92\text{x}10^{-5}$	$2.89\text{x}10^{-4}$	$9.71\text{x}10^{-2}$
rs75	$9.93\text{x}10^{-5}$	$7.02\text{x}10^{-3}$	$4.77\text{x}10^{-2}$
.	.	.	.
.	.	.	.
.	.	.	.

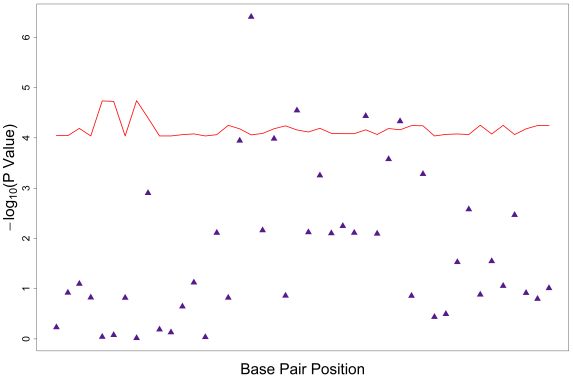
Step 1: Identifying Noteworthy Associations (R_1). SNPs (grey) above the association threshold (green line) are considered noteworthy, there are 5 noteworthy associations here.



SNP	R_1 Threshold	P-value R_1	P-value I_M
rs88	$1.03\text{x}10^{-4}$	$7.48\text{x}10^{-5}$	$\mathbf{1.31\text{x}10^{-5}}$
rs99	$1.12\text{x}10^{-4}$	$9.81\text{x}10^{-5}$	$\mathbf{7.18\text{x}10^{-5}}$
rs48	$1.22\text{x}10^{-4}$	$1.10\text{x}10^{-6}$	$8.33\text{x}10^{-3}$
rs46	$1.18\text{x}10^{-4}$	$1.85\text{x}10^{-6}$	$8.78\text{x}10^{-3}$
rs43	$1.09\text{x}10^{-4}$	$3.48\text{x}10^{-6}$	$9.22\text{x}10^{-3}$
rs70	$9.69\text{x}10^{-5}$	$8.85\text{x}10^{-2}$	$1.98\text{x}10^{-2}$
rs74	$1.02\text{x}10^{-4}$	$9.49\text{x}10^{-2}$	$1.21\text{x}10^{-2}$
.	.	.	.
.	.	.	.
.	.	.	.

Step 2: For Noteworthy SNPs Investigate Imprinting Effects (I_M). Each SNP has an association -$\log_{10}$(P-value) (grey) and an imprinting -$\log_{10}$(P-value) (blue). Noteworthy imprinting SNPs are those SNPs (blue) with both an imprinting -$\log_{10}$(P-value) and an association -$\log_{10}$(P-value) above the threshold (green line).

Figure S2: Identifying Noteworthy Imprinting Effects using the Bayesian Threshold



SNP	S_1 Threshold	P-value S_1
rs202	$1.12\text{x}10^{-4}$	$\mathbf{8.79\text{x}10^{-7}}$
rs808	$9.89\text{x}10^{-5}$	$\mathbf{6.56\text{x}10^{-5}}$
rs303	$9.23\text{x}10^{-5}$	$\mathbf{7.55\text{x}10^{-5}}$
rs707	$8.62\text{x}10^{-5}$	$\mathbf{8.07\text{x}10^{-5}}$
rs606	$1.01\text{x}10^{-4}$	$2.34\text{x}10^{-4}$
rs404	$1.11\text{x}10^{-4}$	$2.92\text{x}10^{-4}$
rs909	$9.91\text{x}10^{-5}$	$4.15\text{x}10^{-3}$
.	.	.
.	.	.
.	.	.

Figure S3: Identifying Maternal Genetic Effects Using the Bayesian Threshold.
SNPs (purple) above the maternal genetic threshold (red line) are considered noteworthy, there are 4 noteworthy maternal genetic effects (S_1) here.

Sensitivity of Bayesian Threshold

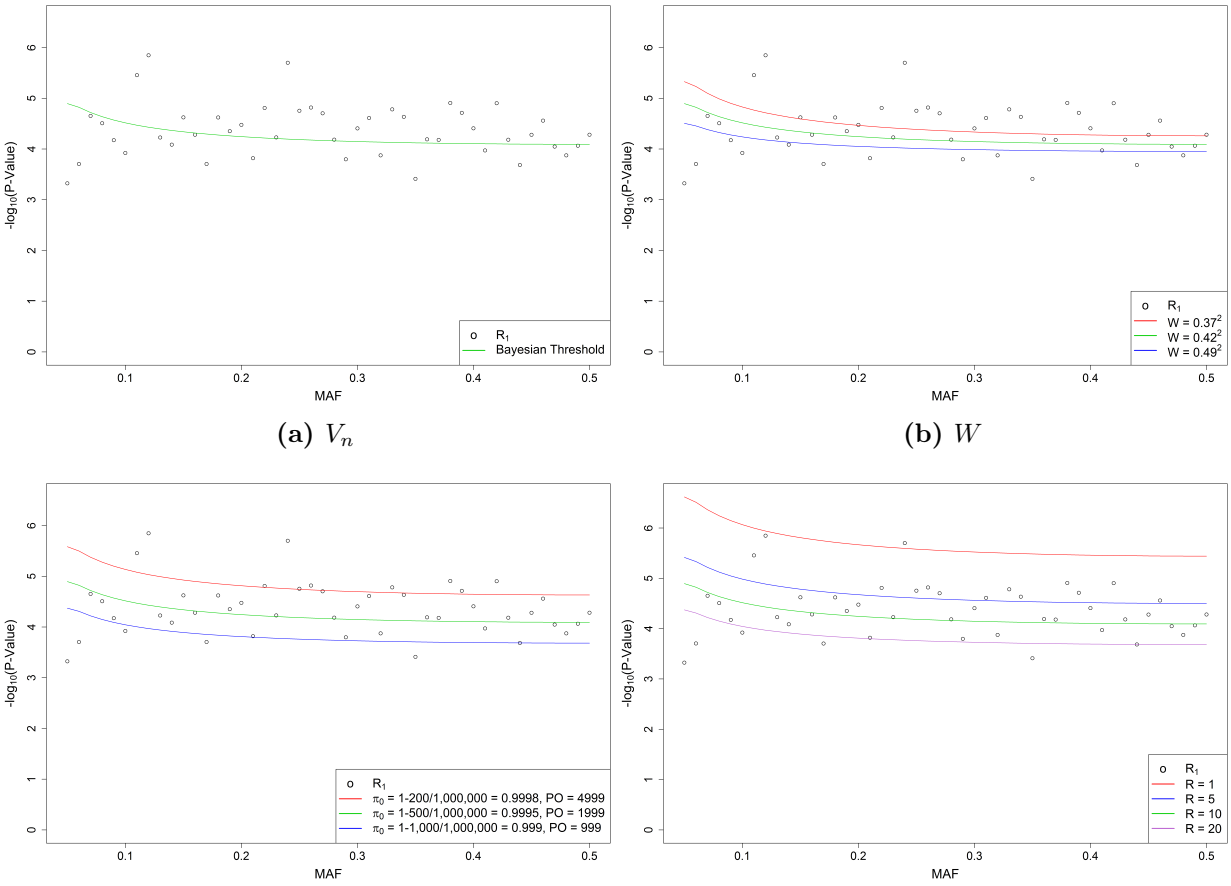
The standard error (V_n) is controlled/determined by the sample size and MAF for the offspring genetic effect parameter, R_1, and the maternal genetic parameter, S_1. The sample size does not vary to any great extent from SNP to SNP (only changes if all 3 family members have missing data at a SNP, otherwise missing data is estimated by EMIM) but the MAF does vary and we examined what happens to the threshold as the MAF varies in Figure S4(a) using the sample size from our smallest dataset (AGP Strict, n = 1,594). There is a higher threshold at low MAFs, which is to be expected as there is less information here to determine a noteworthy finding and thus the threshold needs to be more stringent, and once the MAF > 0.2 there is not much change in the threshold, and can be seen to level out.

Given that there are several hundred to a thousand loci that are likely to contribute to ASD [17–19], we tested π_0 = 1 - 200/1 000 000 = 0.9998 $\Rightarrow$ PO = 4 999, π_0 = 1 - 500/1 000 000 = 0.9995 $\Rightarrow$ PO = 1 999 and π_0 = 1 - 1 000/1 000 000 = 0.999 $\Rightarrow$ PO = 999 corresponding to roughly 200, 500 and 1,000 contributing loci, respectively, see Figure S4(c). We can see from this plot that the threshold is more sensitive to changes in PO than to changes in W and as would be expected, the stronger the belief that there are more associations to find the lower the Bayesian threshold.

We investigated the sensitivity to different R parameter values (ratio of cost of type II errors to type I errors) of our model, see Figure S4(d). This plot shows that the threshold is much higher for R = 1 (where cost of type I errors is equal to the cost of type II errors), as would be expected. Given the limited power to detect parent-of-origin effects and that EMIM is somewhat conservative at low MAFs [5], we felt that R = 1 is not appropriate for our model. Also, Wakefield [21] compared the Bayesian threshold versus the Bonferroni correction. For sample sizes ranging between 1,000 -

3,000 (which compared roughly to the sample sizes in our datasets) and using $W = 0.42^2$ together with π_0 = 1 - 1/100,000, which is weaker than our belief of 1 - 500/1 000 000, found that for R = 10, there were at most 2 false discoveries for approximately every 10 extra findings using the Bayesian threshold. This seems very beneficial in our model.

Therefore, we felt our choice of parameters (the green line in Figure S4, where V_n is the standard error, $W = 0.42^2$, π_0 = 1 - 500/1,000,000 and R = 10) for our Bayesian threshold for R_1 and S_1 were appropriate for the approach in EMIM with the ASD datasets we are analysing here.



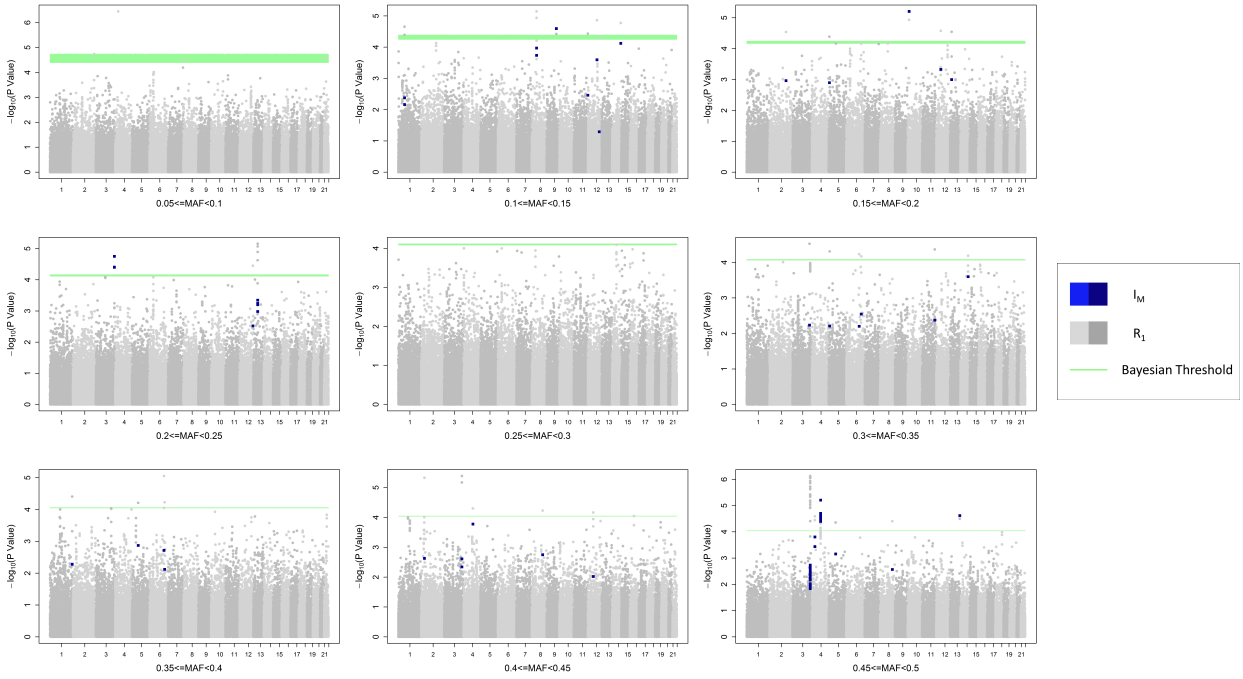
(a) V_n **(b)** W

(c) PO **(d)** R

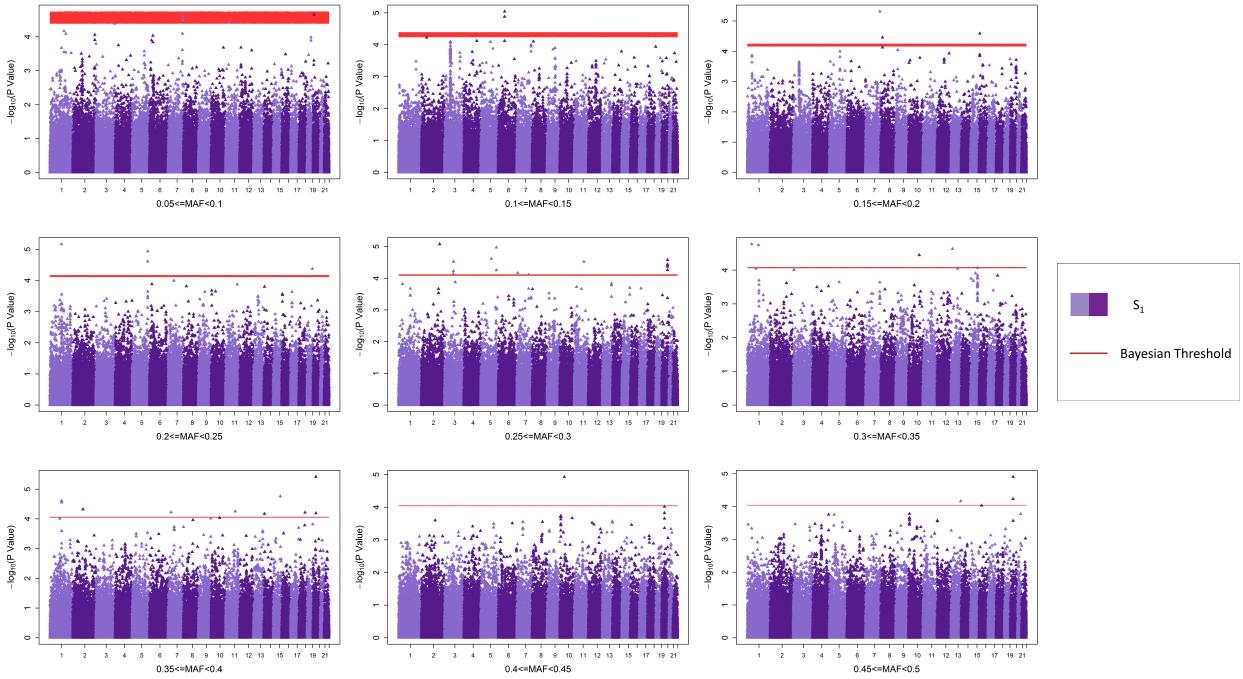
Figure S4: Sensitivity of the Bayesian Threshold, where V_n is the standard error that depends on MAF and sample size (n =1,594 here), $W = 0.42^2$, π_0 = 1 - 500/1,000,000 (PO = 1,999) and R = 10, unless otherwise stated

Results

AGP Spectrum Results



(a) Imprinting



(b) Maternal Genetic Effects

Figure S5: Manhattan Plots for Imprinting (Figure S5 (a)) and Maternal Genetic Effects (Figure S5 (b)) for Spectrum Phenotype in the AGP Dataset

Table S4: Imprinting Results in the AGP Spectrum dataset & corresponding findings in the SSC Spectrum dataset

AGP Results											SSC Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	R_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs675680	4	0.06	0.52	$3.58\text{x}10^{-7}$	0.64	$1.77\text{x}10^{-4}$	2.36	$3.02\text{x}10^{-6}$	$3.20\text{x}10^{-5}$	NA	rs675680	1	0.06	1.15	0.28	1.25	0.07	0.81	0.24
rs10025482	4	0.49	1.33	$4.49\text{x}10^{-5}$	1.29	$3.71\text{x}10^{-4}$	0.59	$6.21\text{x}10^{-6}$	$1.05\text{x}10^{-4}$	*C4orf37*	rs6854802	1	0.48	0.93	0.28	0.88	0.07	1.19	0.15
rs11256141	10	0.16	0.69	$1.17\text{x}10^{-5}$	0.74	$1.98\text{x}10^{-4}$	1.77	$6.23\text{x}10^{-6}$	$7.36\text{x}10^{-5}$	*LINC00709*	rs11256141	1	0.16	0.93	0.37	1.08	0.34	0.95	0.71
rs1491994	3	0.24	0.73	$1.82\text{x}10^{-5}$	0.83	$1.06\text{x}10^{-2}$	1.63	$1.76\text{x}10^{-5}$	$8.90\text{x}10^{-5}$	*CLDN16*	NA	0							
rs2031836	13	0.46	1.34	$3.16\text{x}10^{-5}$	1.32	$6.83\text{x}10^{-5}$	0.62	$2.41\text{x}10^{-5}$	$1.05\text{x}10^{-4}$	NA	rs2031836	1	0.46	0.96	0.55	1.00	0.98	1.10	0.42
rs17683817	5	0.16	1.40	$6.85\text{x}10^{-5}$	1.30	$2.48\text{x}10^{-3}$	0.58	$2.45\text{x}10^{-5}$	$7.31\text{x}10^{-5}$	*WDR41*	rs17683817	1	0.15	0.90	0.19	0.77	0.00	1.23	0.12
rs10491726	9	0.12	0.68	$3.78\text{x}10^{-5}$	0.76	$2.58\text{x}10^{-3}$	1.81	$2.55\text{x}10^{-5}$	$5.97\text{x}10^{-5}$	*PTGR1*	rs10491726	1	0.10	0.89	0.23	0.87	0.17	1.22	0.18
rs807566	14	0.15	0.69	$1.69\text{x}10^{-5}$	0.72	$1.61\text{x}10^{-4}$	1.69	$7.57\text{x}10^{-5}$	$7.63\text{x}10^{-5}$	*BCL11B*	rs807566	1	0.14	1.01	0.88	1.09	0.34	0.92	0.55
rs9671845	14	0.29	0.75	$8.12\text{x}10^{-5}$	0.81	$3.22\text{x}10^{-3}$	1.57	$8.22\text{x}10^{-5}$	$9.55\text{x}10^{-5}$	NA	rs10139853	0.96	0.30	1.00	0.98	0.97	0.66	1.05	0.66

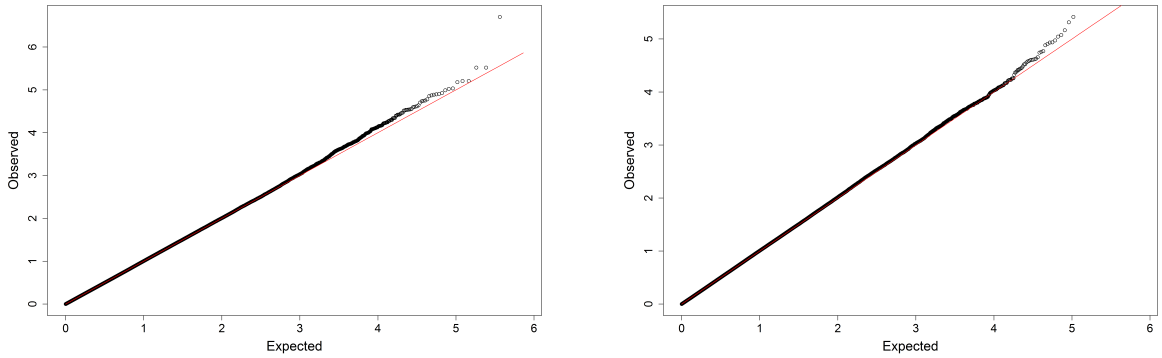
R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

Table S5: Maternal Genetic Effects Results in the AGP Spectrum dataset & corresponding findings in the SSC Spectrum dataset

AGP Results											SSC Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	S_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs2268949	20	0.39	1.26	$1.40\text{x}10^{-3}$	1.39	$3.84\text{x}10^{-6}$	0.68	$6.32\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	NA	rs2268949	1	0.38	0.92	0.25	0.98	0.77	1.14	0.26
rs6965442	7	0.19	1.31	$1.00\text{x}10^{-3}$	1.45	$4.85\text{x}10^{-6}$	0.69	$1.92\text{x}10^{-3}$	$8.16\text{x}10^{-5}$	*LOC729986*	rs6965442	1	0.18	1.07	0.4	1.01	0.87	0.87	0.27
rs6677933	1	0.2	0.76	$3.20\text{x}10^{-4}$	0.71	$6.83\text{x}10^{-6}$	1.63	$5.02\text{x}10^{-5}$	$8.20\text{x}10^{-5}$	NA	rs6677933	1	0.21	1.01	0.9	0.99	0.85	1.09	0.47
rs4637047	2	0.25	0.84	$1.21\text{x}10^{-2}$	0.72	$8.40\text{x}10^{-6}$	1.33	$1.20\text{x}10^{-2}$	$9.03\text{x}10^{-5}$	NA	NA	0							
rs9462733	6	0.15	1.21	$4.56\text{x}10^{-2}$	1.49	$9.02\text{x}10^{-6}$	0.69	$6.02\text{x}10^{-3}$	$6.99\text{x}10^{-5}$	NA	NA	0							
rs4516878	5	0.24	1.21	$1.43\text{x}10^{-2}$	1.4	$1.16\text{x}10^{-5}$	0.72	$4.37\text{x}10^{-3}$	$8.94\text{x}10^{-5}$	*CTC-340A15.2*	rs4516878	1	0.25	1.11	0.17	1.07	0.37	0.9	0.39
rs1617306	10	0.45	1.2	$6.80\text{x}10^{-3}$	1.35	$1.17\text{x}10^{-5}$	0.69	$9.90\text{x}10^{-4}$	$1.05\text{x}10^{-4}$	NA	rs1617306	1	0.45	1.01	0.83	1.07	0.32	0.97	0.81
rs9283909	6	0.11	1.29	$1.16\text{x}10^{-2}$	1.53	$1.31\text{x}10^{-5}$	0.59	$2.36\text{x}10^{-4}$	$5.82\text{x}10^{-5}$	NA	rs12526543	1	0.1	0.97	0.75	0.93	0.47	1.06	0.68
rs2982502	1	0.3	0.92	$2.24\text{x}10^{-1}$	0.74	$1.70\text{x}10^{-5}$	1.31	$1.50\text{x}10^{-2}$	$9.64\text{x}10^{-5}$	*ZFP69B*	rs2982502	1	0.32	1.13	0.08	1.14	0.07	0.78	0.03
rs6496603	15	0.4	1.19	$1.48\text{x}10^{-2}$	1.35	$1.75\text{x}10^{-5}$	0.69	$8.69\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	*ANPEP*	NA	0							
rs1277203	1	0.33	0.77	$2.17\text{x}10^{-4}$	0.74	$1.81\text{x}10^{-5}$	1.62	$1.67\text{x}10^{-5}$	$9.95\text{x}10^{-5}$	*AKNAD1*	rs1277203	1	0.35	1.03	0.71	0.93	0.31	1.02	0.87
rs8113869	20	0.09	0.9	$2.71\text{x}10^{-1}$	0.64	$2.21\text{x}10^{-5}$	1.51	$6.04\text{x}10^{-3}$	$4.68\text{x}10^{-5}$	*LINC00658*	rs8113869	1	0.1	0.95	0.6	0.93	0.49	1.19	0.24
rs2183284	13	0.32	0.82	$4.58\text{x}10^{-3}$	0.74	$2.35\text{x}10^{-5}$	1.43	$1.75\text{x}10^{-3}$	$9.88\text{x}10^{-5}$	*LINC00426*	rs2183284	1	0.35	1.02	0.78	0.99	0.94	1.04	0.72
rs3891371	5	0.25	0.8	$1.71\text{x}10^{-3}$	0.73	$2.42\text{x}10^{-5}$	1.68	$6.59\text{x}10^{-6}$	$9.07\text{x}10^{-5}$	*KCNN2*	NA	0							
rs7778273	7	0.08	1.34	$9.50\text{x}10^{-3}$	1.6	$2.52\text{x}10^{-5}$	0.55	$1.94\text{x}10^{-4}$	$4.51\text{x}10^{-5}$	*CUL1*	rs7778273	1	0.08	1	0.97	1.05	0.69	1.03	0.88
rs3848375	16	0.18	0.81	$7.13\text{x}10^{-3}$	0.72	$2.59\text{x}10^{-5}$	1.37	$9.19\text{x}10^{-3}$	$7.82\text{x}10^{-5}$	*MGRN1*	rs3848374	0.96	0.2	0.91	0.22	0.86	0.06	1.22	0.1
rs6021903	20	0.26	0.86	$3.91\text{x}10^{-2}$	0.74	$2.66\text{x}10^{-5}$	1.46	$9.71\text{x}10^{-4}$	$9.19\text{x}10^{-5}$	*LINC01524*	rs968162	1	0.27	1.05	0.52	0.96	0.58	0.93	0.56
rs1766862	1	0.39	0.79	$6.90\text{x}10^{-4}$	0.75	$2.78\text{x}10^{-5}$	1.47	$3.81\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	*LRIG2*	rs1766862	1	0.41	0.84	0.01	0.87	0.05	1.34	0.01
rs545208	11	0.25	0.83	$8.35\text{x}10^{-3}$	0.74	$3.00\text{x}10^{-5}$	1.39	$4.70\text{x}10^{-3}$	$9.10\text{x}10^{-5}$	*MAML2*	rs545208	1	0.26	0.98	0.8	1.02	0.81	1.01	0.93
rs2978880	8	0.18	0.79	$2.75\text{x}10^{-3}$	0.72	$3.49\text{x}10^{-5}$	1.45	$2.42\text{x}10^{-3}$	$7.90\text{x}10^{-5}$	*DEFB1*	rs2978880	1	0.2	0.89	0.16	0.97	0.69	1.04	0.73
rs2060792	10	0.31	0.88	$5.83\text{x}10^{-2}$	0.74	$3.59\text{x}10^{-5}$	1.31	$1.92\text{x}10^{-2}$	$9.72\text{x}10^{-5}$	*RP11-34D15.2*	rs2060792	1	0.32	1.06	0.45	0.98	0.82	1.12	0.34
rs7128766	11	0.07	1.03	$8.01\text{x}10^{-1}$	1.64	$3.82\text{x}10^{-5}$	0.73	$7.56\text{x}10^{-2}$	$3.99\text{x}10^{-5}$	*NELL1*	rs7128766	1	0.08	0.98	0.83	0.96	0.72	1.01	0.97
rs10409120	19	0.23	0.86	$3.77\text{x}10^{-2}$	0.73	$4.20\text{x}10^{-5}$	1.61	$5.22\text{x}10^{-5}$	$8.84\text{x}10^{-5}$	*ZNF83*	rs10409120	1	0.23	1.04	0.59	1.15	0.08	0.91	0.44
rs11674199	2	0.37	0.86	$2.94\text{x}10^{-2}$	0.75	$4.75\text{x}10^{-5}$	1.42	$3.42\text{x}10^{-3}$	$1.02\text{x}10^{-4}$	*NPAS2*	rs11674199	1	0.37	1.01	0.85	1.06	0.38	0.93	0.48
rs1978763	11	0.34	0.83	$9.16\text{x}10^{-3}$	0.75	$5.58\text{x}10^{-5}$	1.38	$5.08\text{x}10^{-3}$	$1.00\text{x}10^{-4}$	*MAML2*	rs1978763	1	0.35	0.94	0.38	0.97	0.65	1.08	0.5
rs12622230	2	0.14	1.22	$3.14\text{x}10^{-2}$	1.44	$5.93\text{x}10^{-5}$	0.69	$5.47\text{x}10^{-3}$	$6.65\text{x}10^{-5}$	NA	rs12622230	1	0.13	0.97	0.77	1.08	0.42	0.97	0.85
rs1174939	7	0.35	0.88	$5.22\text{x}10^{-2}$	0.76	$5.98\text{x}10^{-5}$	1.38	$3.62\text{x}10^{-3}$	$1.01\text{x}10^{-4}$	NA	rs1174939	1	0.36	0.96	0.55	0.92	0.23	1.2	0.11
rs9959847	18	0.36	1.21	$5.75\text{x}10^{-3}$	1.31	$6.09\text{x}10^{-5}$	0.68	$3.48\text{x}10^{-4}$	$1.02\text{x}10^{-4}$	NA	rs9959847	1	0.37	0.92	0.27	0.91	0.21	1.15	0.24
rs7150691	14	0.39	1.19	$1.16\text{x}10^{-2}$	1.32	$6.73\text{x}10^{-5}$	0.69	$9.41\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	*TRAV37*	rs7150691	1	0.39	1.08	0.31	1.03	0.67	0.94	0.59
rs10486157	7	0.28	0.76	$1.17\text{x}10^{-4}$	0.75	$6.79\text{x}10^{-5}$	1.69	$3.03\text{x}10^{-6}$	$9.49\text{x}10^{-5}$	NA	rs10486157	1	0.28	0.96	0.56	0.89	0.11	1.08	0.49
rs2031836	13	0.47	1.34	$3.16\text{x}10^{-5}$	1.32	$6.83\text{x}10^{-5}$	0.62	$2.41\text{x}10^{-5}$	$1.05\text{x}10^{-4}$	NA	rs2031836	1	0.46	0.96	0.55	1	0.98	1.1	0.42
rs9870610	3	0.28	1.16	$4.62\text{x}10^{-2}$	1.33	$7.24\text{x}10^{-5}$	0.71	$3.09\text{x}10^{-3}$	$9.47\text{x}10^{-5}$	*ROBO2*	rs9870610	1	0.25	1.03	0.7	1.16	0.05	0.86	0.2
rs11975640	7	0.28	0.92	$2.07\text{x}10^{-1}$	0.75	$7.70\text{x}10^{-5}$	1.37	$6.13\text{x}10^{-3}$	$9.45\text{x}10^{-5}$	*SPAM1*	rs11975640	1	0.31	0.91	0.2	0.82	0.01	1.27	0.04
rs4885749	13	0.33	1.2	$1.08\text{x}10^{-2}$	1.32	$8.97\text{x}10^{-5}$	0.67	$5.08\text{x}10^{-4}$	$9.90\text{x}10^{-5}$	NA	rs4885749	1	0.32	1.06	0.42	0.96	0.54	1	1
rs2066197	1	0.34	0.78	$1.55\text{x}10^{-4}$	0.77	$8.99\text{x}10^{-5}$	1.42	$9.49\text{x}10^{-4}$	$1.00\text{x}10^{-4}$	NA	rs2066197	1	0.33	1.22	0.01	1.14	0.07	0.76	0.02
rs7921660	10	0.39	0.8	$1.22\text{x}10^{-3}$	0.77	$9.25\text{x}10^{-5}$	1.59	$1.81\text{x}10^{-5}$	$1.03\text{x}10^{-4}$	NA	rs7921660	1	0.38	1	0.98	1.03	0.66	1.03	0.78
rs1908211	16	0.44	0.88	$6.02\text{x}10^{-2}$	0.76	$9.31\text{x}10^{-5}$	1.38	$5.31\text{x}10^{-3}$	$1.05\text{x}10^{-4}$	NA	NA	0							
rs28498266	9	0.38	0.91	$1.93\text{x}10^{-1}$	0.76	$9.52\text{x}10^{-5}$	1.34	$1.02\text{x}10^{-2}$	$1.02\text{x}10^{-4}$	*RNU6ATAC*	rs28498266	1	0.39	1.22	0.01	1.18	0.02	0.73	0.01
rs1245481	1	0.4	1.25	$1.09\text{x}10^{-3}$	1.31	$9.72\text{x}10^{-5}$	0.66	$1.77\text{x}10^{-4}$	$1.04\text{x}10^{-4}$	*LINC01057*	rs1245481	1	0.38	0.94	0.4	1.02	0.82	1.05	0.66
rs4684385	3	0.35	1.17	$2.07\text{x}10^{-2}$	1.31	$9.86\text{x}10^{-5}$	0.71	$1.43\text{x}10^{-3}$	$1.01\text{x}10^{-4}$	NA	rs4684385	1	0.34	1.13	0.1	1.09	0.24	0.85	0.18

R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

Figure S6 gives the QQ plots for I_M and S_1 in the AGP Spectrum dataset.



(a) I_M (b) S_1

Figure S6: QQ plots for AGP Spectrum dataset

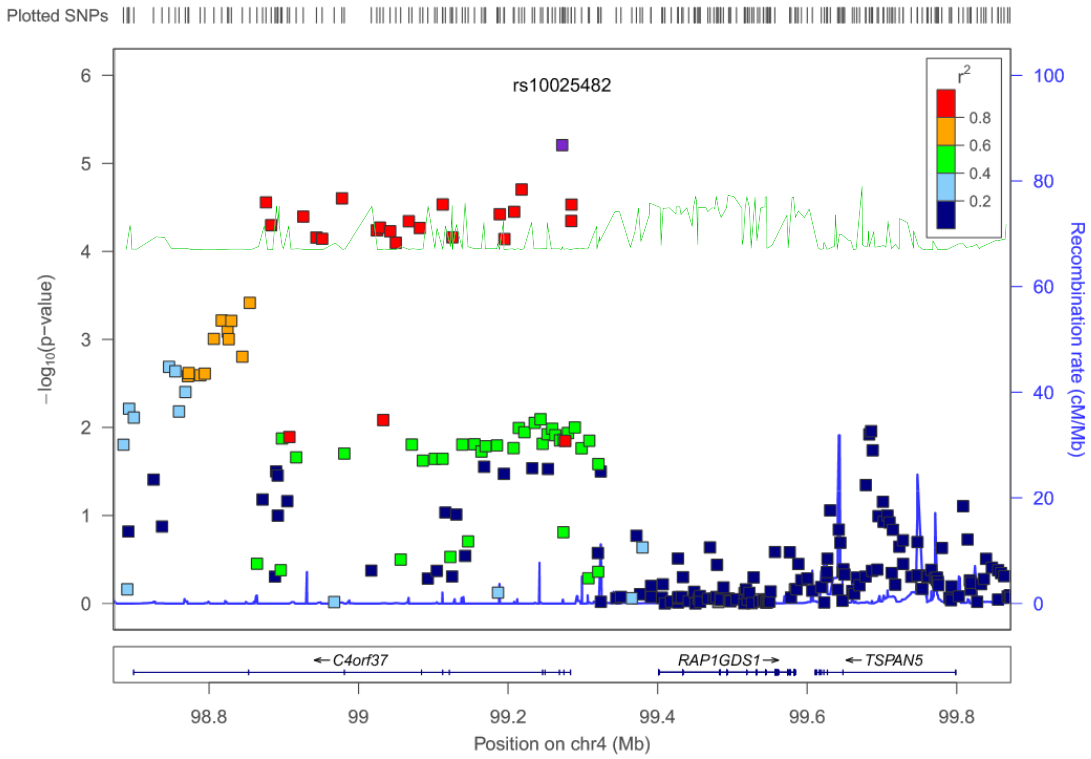


Figure S7: AGP Spectrum Chromosome 4, rs10025482 Paternal Over-Transmission. Regional plot of SNPs highlighted in the AGP Spectrum analysis for imprinting result when the association is above the Bayesian threshold for R_1 (green line). Index SNP rs10025482 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue.

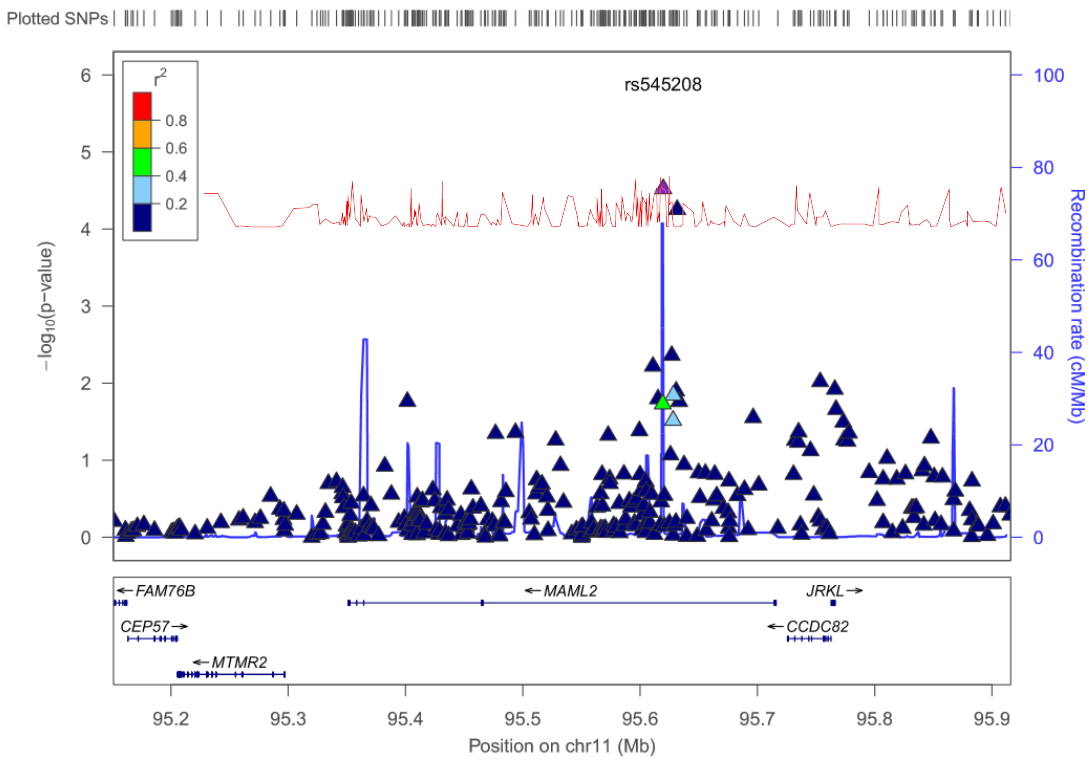


Figure S8: AGP Spectrum Chromosome 11, rs545208 Maternal Genetic Effect. Regional plot of SNPs highlighted in the AGP Spectrum analysis for maternal genetic effects (S_1, triangles). Index SNP rs545208 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue. The red line represents the Bayesian threshold for S_1.

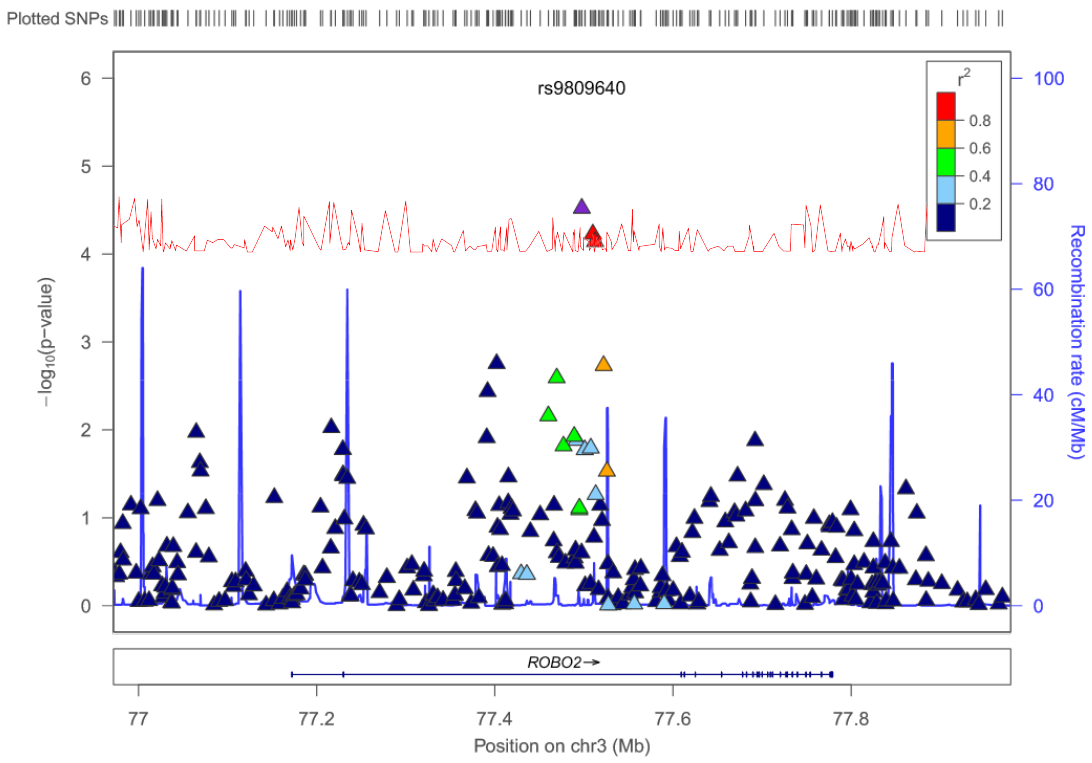


Figure S9: AGP Spectrum Chromosome 3, rs9809640 Maternal Genetic Effect. Regional plot of SNPs highlighted in the AGP Spectrum analysis for maternal genetic effects (S_1, triangles). Index SNP rs9809640 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue. The red line represents the Bayesian threshold for S_1.

AGP Strict Results

There were seven noteworthy imprinting results and there were forty-eight independent loci with a maternal genetic effect above the S_1 threshold (four of which overlap with AGP Spectrum results), see the Manhattan plots (Figure S10) and Tables S6 and S7 for all hits that were above the threshold for offspring genetic effects (R_1) and imprinting (I_M) or were above the threshold for maternal genetic effects (S_1). Figure S15 gives an the overlap of findings that where above the threshold in both the AGP Strict and AGP Spectrum. (Note that many findings where above the threshold in one of the phenotypes and close but not above the threshold in the other phenotype

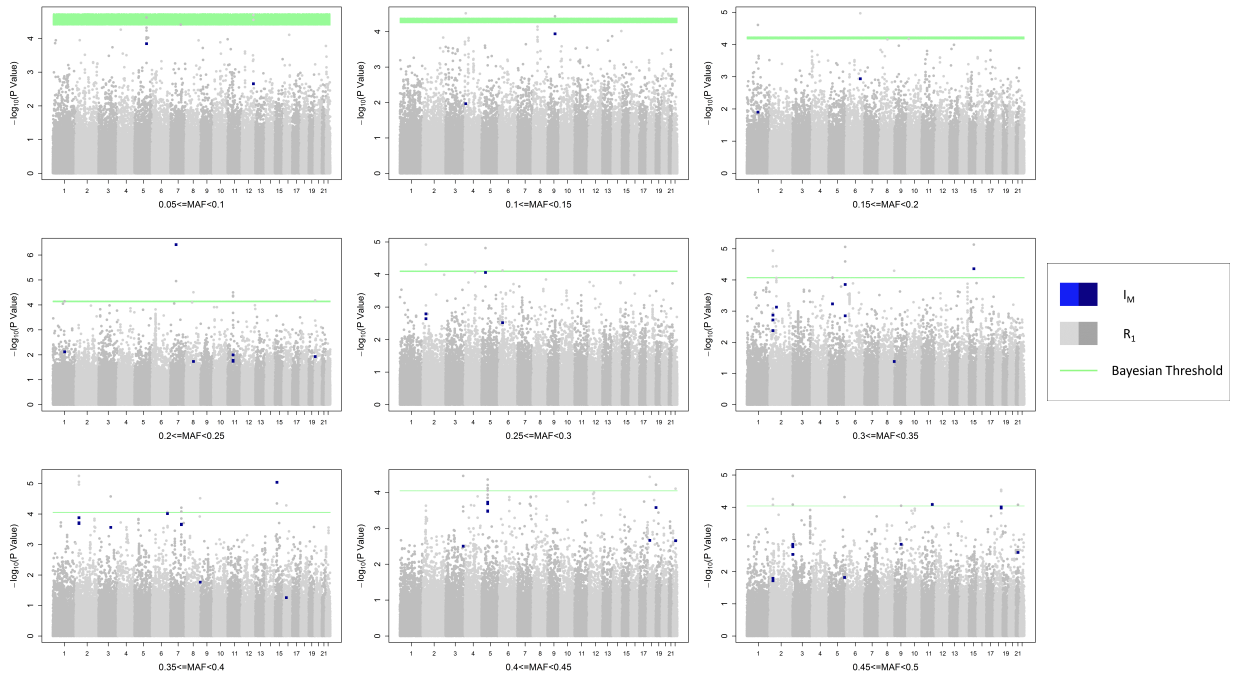
and hence. were not considered to be noteworthy findings.) Figure S14 gives the QQ plots for I_M and S_1 in the AGP Strict dataset.

Imprinting Results

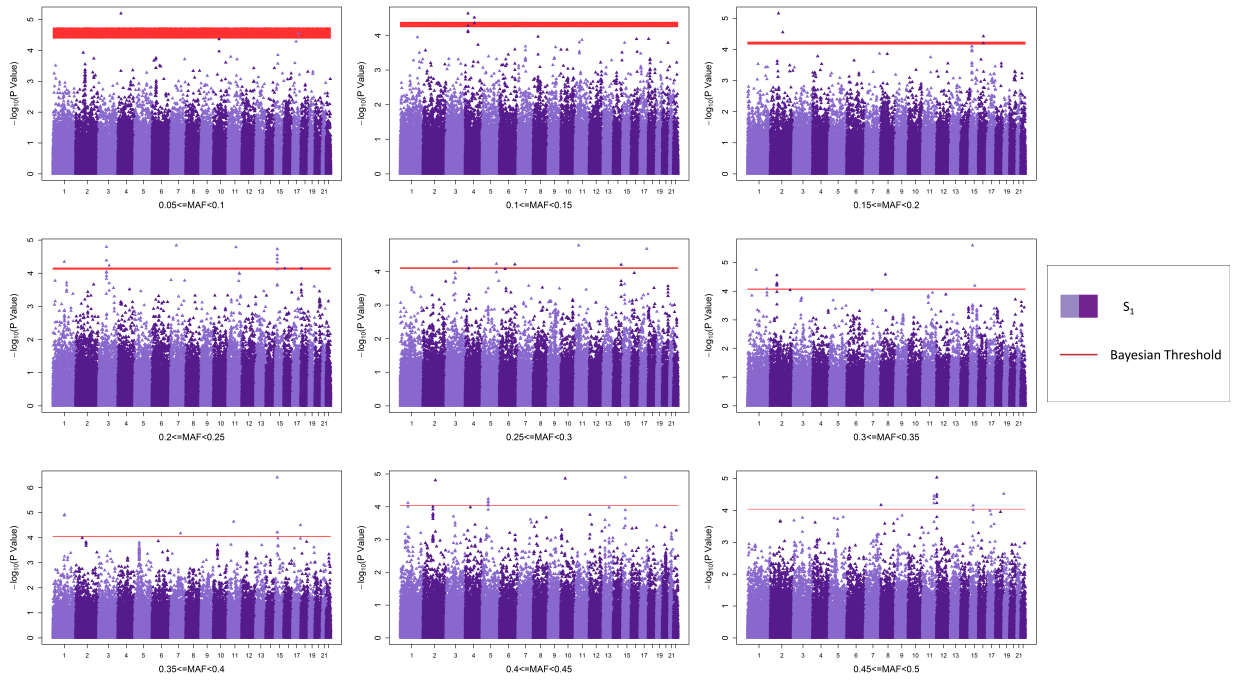
Our strongest associations showed evidence for paternal over-transmission and a maternal genetic effect on chromosome 7p in an intergenic region between *LOC100419776* and *EPS15P1* (rs1525240, $I_M = 0.47$, Wald p-value =3.8x10^{-7}, $S_1 = 1.53$, Wald p-value = 1.4x10^{-5}, see Figure S11). This region was previously linked with a *de novo* mutation in ASD [22]. One of our top hits for maternal over-transmission on chromosome 18 between *DSEL* and *LOC100129135* (rs395393, $I_M = 1.73$, Wald p-value = 9.81x10^{-5}, see Figure S12) was previously implicated for maternal genetic effects [23] ($R^2 = 0.235$ between rs395393 and rs7242936), but the authors did not consider imprinting in their analysis which can mimic maternal genetic effects [5, 24]. Note, the maternal genetic effect found at rs7242936 in [23] was found in a merged dataset consisting of AGRE and SSC samples, so there is some overlap of the samples in [23] and ours (as the AGP contains samples from AGRE).

Maternal Genetic Results

We found evidence for a maternal genetic effect and paternal over-transmission on chromosome 15q15.1 in the *MGA* gene (rs16971976, $S_1 = 1.58$, Wald p-value = 3.9x10^{-7}, $I_M = 0.53$, Wald p-value = 9.1x10^{-6}, see Figure S13). This region was previously linked with ASD in a linkage study [25]. Note there is again potential for small overlap with the samples in [25] and ours as [25] analysed the AGRE dataset.



(a) Imprinting



(b) Maternal Genetic Effects

Figure S10: Manhattan Plots for Imprinting (Figure S10 (a)) and Maternal Genetic Effects (Figure S10 (b)) for Strict Phenotype in the AGP Dataset

Table S6: Imprinting Results in the AGP Strict dataset & corresponding findings in the SSC Strict dataset

AGP Results											SSC Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	R_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs1525240	7	0.24	1.53	$1.11\text{x}10^{-5}$	1.52	$1.44\text{x}10^{-5}$	0.47	$3.83\text{x}10^{-7}$	$8.88\text{x}10^{-5}$	NA	rs1525240	1	0.25	0.94	0.49	0.91	0.28	1.23	0.12
rs16971976	15	0.36	1.45	$4.49\text{x}10^{-5}$	1.58	$3.90\text{x}10^{-7}$	0.53	$9.09\text{x}10^{-6}$	$1.01\text{x}10^{-4}$	*MGA*	rs16971976	1	0.37	1.02	0.80	1.08	0.30	0.94	0.61
rs8025806	15	0.31	1.48	$7.37\text{x}10^{-6}$	1.42	$6.40\text{x}10^{-5}$	0.57	$4.37\text{x}10^{-5}$	$9.74\text{x}10^{-5}$	NA	rs8025806	1	0.30	1.10	0.24	1.07	0.42	0.94	0.63
rs1016081	11	0.49	1.42	$7.95\text{x}10^{-5}$	1.33	$1.27\text{x}10^{-3}$	0.56	$8.22\text{x}10^{-5}$	$1.05\text{x}10^{-4}$	NA	rs1016081	1	0.49	0.97	0.72	1.01	0.89	1.04	0.78
rs1423431	5	0.28	1.50	$1.54\text{x}10^{-5}$	1.39	$4.13\text{x}10^{-4}$	0.56	$8.65\text{x}10^{-5}$	$9.46\text{x}10^{-5}$	NA	rs1423431	1	0.27	1.02	0.84	1.18	0.04	0.86	0.24
rs325105	6	0.39	0.70	$8.55\text{x}10^{-5}$	0.73	$3.33\text{x}10^{-4}$	1.76	$9.67\text{x}10^{-5}$	$1.03\text{x}10^{-4}$	NA	rs325105	1	0.39	1.02	0.77	1.04	0.61	0.89	0.37
rs395393	18	0.48	0.69	$2.88\text{x}10^{-5}$	0.79	$5.78\text{x}10^{-3}$	1.73	$9.81\text{x}10^{-5}$	$1.05\text{x}10^{-4}$	NA	rs395393	1	0.48	1.04	0.60	1.00	0.98	0.86	0.26

R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

Table S7: Maternal Genetic Effects Results in the AGP Strict dataset & corresponding findings in the SSC Strict dataset

AGP Results											SSC Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	S_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs16971976	15	0.37	1.45	$4.49\text{x}10^{-5}$	1.58	$3.90\text{x}10^{-7}$	0.53	$9.09\text{x}10^{-6}$	$1.02\text{x}10^{-4}$	*MGA*	rs16971976	1	0.37	1.02	0.80	1.08	0.30	0.94	0.61
rs12591300	15	0.36	1.33	$1.60\text{x}10^{-3}$	1.52	$2.51\text{x}10^{-6}$	0.58	$1.56\text{x}10^{-4}$	$1.02\text{x}10^{-4}$	*FAM227B*	rs10519225	0.90	0.36	1.24	0.01	1.14	0.11	0.76	0.04
rs675680	4	0.05	0.52	$5.49\text{x}10^{-5}$	0.47	$6.30\text{x}10^{-6}$	3.30	$1.10\text{x}10^{-6}$	$2.78\text{x}10^{-5}$	*RP11-123O22.1*	rs675680	1	0.06	1.27	0.08	1.31	0.05	0.73	0.11
rs2559081	2	0.17	1.28	$2.87\text{x}10^{-2}$	1.65	$6.91\text{x}10^{-6}$	0.67	$1.34\text{x}10^{-2}$	$7.63\text{x}10^{-5}$	*DYSF*	rs2559081	1	0.17	1.05	0.58	1.12	0.24	0.84	0.25
rs1044471	12	0.45	0.77	$2.59\text{x}10^{-3}$	0.68	$9.18\text{x}10^{-6}$	1.73	$6.14\text{x}10^{-5}$	$1.05\text{x}10^{-4}$	*ADIPOR2*	rs1044471	1	0.46	0.98	0.81	0.98	0.81	1.12	0.36
rs1778015	1	0.38	0.81	$1.14\text{x}10^{-2}$	0.68	$1.21\text{x}10^{-5}$	1.66	$3.08\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	NA	rs1766862	1	0.41	0.86	0.06	0.87	0.07	1.30	0.05
rs1617306	10	0.45	1.27	$7.99\text{x}10^{-3}$	1.47	$1.37\text{x}10^{-5}$	0.63	$1.60\text{x}10^{-3}$	$1.05\text{x}10^{-4}$	NA	rs1617306	1	0.46	1.03	0.71	1.08	0.34	0.97	0.81
rs1525240	7	0.24	1.53	$1.11\text{x}10^{-5}$	1.52	$1.44\text{x}10^{-5}$	0.47	$3.83\text{x}10^{-7}$	$8.93\text{x}10^{-5}$	NA	rs1525240	1	0.25	0.94	0.49	0.91	0.28	1.23	0.12
rs4611601	2	0.40	0.84	$3.98\text{x}10^{-2}$	0.69	$1.55\text{x}10^{-5}$	1.67	$2.88\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	*MYO7B*	rs4611601	1	0.41	0.90	0.18	0.88	0.10	1.17	0.22
rs7628838	3	0.24	1.29	$8.14\text{x}10^{-3}$	1.51	$1.59\text{x}10^{-5}$	0.63	$1.25\text{x}10^{-3}$	$8.89\text{x}10^{-5}$	*SUCLG2*	rs4856867	0.96	0.21	0.96	0.62	0.96	0.66	1.08	0.56
rs10897779	11	0.21	0.81	$2.30\text{x}10^{-2}$	0.66	$1.63\text{x}10^{-5}$	1.53	$4.43\text{x}10^{-3}$	$8.44\text{x}10^{-5}$	NA	rs10897779	1	0.24	0.97	0.74	1.10	0.25	0.91	0.48
rs7945103	11	0.25	0.78	$5.28\text{x}10^{-3}$	0.68	$1.67\text{x}10^{-5}$	1.65	$3.25\text{x}10^{-4}$	$9.14\text{x}10^{-5}$	NA	rs7945103	1	0.26	1.20	0.03	1.22	0.02	0.74	0.02
rs2066197	1	0.32	0.73	$2.52\text{x}10^{-4}$	0.69	$1.79\text{x}10^{-5}$	1.57	$8.41\text{x}10^{-4}$	$9.88\text{x}10^{-5}$	NA	rs2066197	1	0.33	1.21	0.02	1.07	0.44	0.82	0.14
rs10512561	17	0.31	1.27	$1.12\text{x}10^{-2}$	1.47	$2.12\text{x}10^{-5}$	0.59	$3.71\text{x}10^{-4}$	$9.77\text{x}10^{-5}$	NA	rs10512561	1	0.32	1.03	0.68	1.01	0.87	0.97	0.81
rs1622278	11	0.38	0.86	$7.59\text{x}10^{-2}$	0.68	$2.27\text{x}10^{-5}$	1.56	$2.10\text{x}10^{-3}$	$1.02\text{x}10^{-4}$	*FADS2P1*	rs1622278	1	0.39	1.13	0.12	1.08	0.34	0.80	0.09
rs315688	4	0.14	1.22	$9.48\text{x}10^{-2}$	1.62	$2.30\text{x}10^{-5}$	0.55	$7.87\text{x}10^{-4}$	$6.91\text{x}10^{-5}$	*ZCCHC4*	rs315688	1	0.15	0.99	0.94	1.03	0.76	0.89	0.41
rs7818821	8	0.29	0.77	$2.65\text{x}10^{-3}$	0.69	$2.61\text{x}10^{-5}$	1.64	$3.64\text{x}10^{-4}$	$9.56\text{x}10^{-5}$	*NRG1*	rs7818821	1	0.30	0.97	0.66	0.94	0.43	1.10	0.47
rs1863047	2	0.36	1.33	$1.84\text{x}10^{-3}$	1.47	$2.75\text{x}10^{-5}$	0.63	$1.38\text{x}10^{-3}$	$1.01\text{x}10^{-4}$	NA	rs17188812	0.97	0.35	0.91	0.25	0.93	0.39	1.30	0.04
rs11683368	2	0.21	1.44	$4.01\text{x}10^{-4}$	1.54	$2.79\text{x}10^{-5}$	0.63	$2.13\text{x}10^{-3}$	$8.38\text{x}10^{-5}$	NA	rs11683368	1	0.17	1.07	0.49	1.01	0.92	1.01	0.92
rs3744103	17	0.07	1.70	$1.26\text{x}10^{-3}$	1.95	$2.81\text{x}10^{-5}$	0.46	$5.48\text{x}10^{-4}$	$4.13\text{x}10^{-5}$	*BZRAP1*	NA	0							
rs12981067	19	0.50	1.27	$6.42\text{x}10^{-3}$	1.45	$3.00\text{x}10^{-5}$	0.65	$2.99\text{x}10^{-3}$	$1.05\text{x}10^{-4}$	*PPAP2C*	rs12981067	1	0.46	1.03	0.74	1.10	0.21	0.86	0.22
rs2850343	4	0.10	0.68	$9.14\text{x}10^{-4}$	0.61	$3.04\text{x}10^{-5}$	1.91	$3.53\text{x}10^{-4}$	$5.54\text{x}10^{-5}$	*PPP3CA*	NA	0							
rs9894139	17	0.39	1.29	$2.87\text{x}10^{-3}$	1.43	$3.12\text{x}10^{-5}$	0.62	$3.96\text{x}10^{-4}$	$1.03\text{x}10^{-4}$	*RBFOX3*	rs9894139	1	0.39	0.87	0.07	0.91	0.25	1.28	0.05
rs2462167	11	0.50	1.31	$1.63\text{x}10^{-3}$	1.43	$3.49\text{x}10^{-5}$	0.66	$3.38\text{x}10^{-3}$	$1.05\text{x}10^{-4}$	NA	rs1403947	1	0.49	1.02	0.84	0.98	0.80	0.96	0.73
rs2161655	16	0.16	0.84	$7.76\text{x}10^{-2}$	0.65	$3.77\text{x}10^{-5}$	1.70	$7.80\text{x}10^{-4}$	$7.24\text{x}10^{-5}$	NA	rs2161655	1	0.17	0.86	0.11	0.90	0.25	1.21	0.16
rs12258303	10	0.08	1.47	$1.12\text{x}10^{-2}$	1.81	$4.29\text{x}10^{-5}$	0.48	$5.98\text{x}10^{-4}$	$4.59\text{x}10^{-5}$	*RP11-556E13.1*	rs16932605	0.91	0.09	1.37	0.01	1.12	0.34	0.67	0.02
rs6677933	1	0.19	0.73	$1.57\text{x}10^{-3}$	0.67	$4.49\text{x}10^{-5}$	1.77	$2.08\text{x}10^{-4}$	$8.11\text{x}10^{-5}$	*LINC01160*	rs6677933	1	0.21	1.04	0.65	1.04	0.69	1.01	0.93
rs7431430	3	0.30	1.28	$7.80\text{x}10^{-3}$	1.45	$5.06\text{x}10^{-5}$	0.56	$6.41\text{x}10^{-5}$	$9.69\text{x}10^{-5}$	NA	rs7431430	1	0.29	0.93	0.39	0.94	0.43	1.01	0.96
rs34978	5	0.43	1.42	$7.67\text{x}10^{-5}$	1.43	$5.72\text{x}10^{-5}$	0.58	$1.87\text{x}10^{-4}$	$1.04\text{x}10^{-4}$	*NLN*	rs1734262	0.81	0.50	1.05	0.50	1.02	0.77	0.82	0.10
rs6868044	5	0.30	1.38	$4.29\text{x}10^{-4}$	1.44	$5.90\text{x}10^{-5}$	0.54	$2.04\text{x}10^{-5}$	$9.68\text{x}10^{-5}$	*GALNT10*	rs6868044	1	0.30	0.97	0.69	1.08	0.34	1.00	0.98
rs2277537	15	0.41	1.32	$2.34\text{x}10^{-3}$	1.43	$6.11\text{x}10^{-5}$	0.61	$8.41\text{x}10^{-4}$	$1.04\text{x}10^{-4}$	*TYRO3*	rs2277537	1	0.43	1.00	0.96	1.00	0.97	1.11	0.43
rs1983635	6	0.31	1.24	$2.08\text{x}10^{-2}$	1.46	$6.18\text{x}10^{-5}$	0.67	$5.89\text{x}10^{-3}$	$9.79\text{x}10^{-5}$	*GRM1*	rs1983635	1	0.28	0.85	0.05	0.82	0.02	1.23	0.12
rs17129021	14	0.29	0.79	$7.95\text{x}10^{-3}$	0.70	$6.30\text{x}10^{-5}$	1.69	$2.12\text{x}10^{-4}$	$9.52\text{x}10^{-5}$	*UNC79*	rs6575325	0.89	0.29	1.07	0.38	0.97	0.68	0.96	0.75
rs8025806	15	0.31	1.48	$7.37\text{x}10^{-6}$	1.42	$6.40\text{x}10^{-5}$	0.57	$4.37\text{x}10^{-5}$	$9.80\text{x}10^{-5}$	*PCAT29*	rs8025806	1	0.30	1.10	0.24	1.07	0.42	0.94	0.63
rs1476652	7	0.39	0.85	$6.47\text{x}10^{-2}$	0.71	$6.61\text{x}10^{-5}$	1.80	$2.61\text{x}10^{-5}$	$1.03\text{x}10^{-4}$	*COL26A1*	NA	0							
rs714650	8	0.44	0.84	$4.15\text{x}10^{-2}$	0.71	$6.76\text{x}10^{-5}$	1.32	$4.17\text{x}10^{-2}$	$1.05\text{x}10^{-4}$	*RP11-134O21.1*	NA	0							
rs12594729	15	0.48	1.28	$4.40\text{x}10^{-3}$	1.42	$6.97\text{x}10^{-5}$	0.56	$4.69\text{x}10^{-5}$	$1.05\text{x}10^{-4}$	NA	NA	0							
rs1036815	18	0.20	0.89	$2.31\text{x}10^{-1}$	0.67	$7.16\text{x}10^{-5}$	1.46	$1.44\text{x}10^{-2}$	$8.21\text{x}10^{-5}$	*SMCHD1*	rs8092725	0.86	0.23	0.99	0.88	1.01	0.95	1.06	0.65
rs12600284	16	0.23	1.36	$2.00\text{x}10^{-3}$	1.47	$7.18\text{x}10^{-5}$	0.61	$1.03\text{x}10^{-3}$	$8.87\text{x}10^{-5}$	*RBFOX1*	rs12600284	1	0.22	0.94	0.45	0.98	0.82	1.07	0.61
rs11163185	1	0.42	0.82	$2.23\text{x}10^{-2}$	0.71	$7.52\text{x}10^{-5}$	1.52	$2.28\text{x}10^{-3}$	$1.04\text{x}10^{-4}$	*SLC44A5*	NA	0							
rs13120537	4	0.27	0.77	$3.58\text{x}10^{-3}$	0.70	$8.02\text{x}10^{-5}$	1.55	$2.33\text{x}10^{-3}$	$9.37\text{x}10^{-5}$	*ARAP2*	NA	0							
rs1048126	1	0.31	0.71	$1.78\text{x}10^{-4}$	0.70	$8.22\text{x}10^{-5}$	1.82	$3.45\text{x}10^{-5}$	$9.77\text{x}10^{-5}$	*GPATCH2*	rs1048126	1	0.32	0.94	0.49	0.92	0.33	1.12	0.39
rs4711453	6	0.28	0.80	$1.26\text{x}10^{-2}$	0.69	$8.38\text{x}10^{-5}$	1.69	$3.93\text{x}10^{-4}$	$9.44\text{x}10^{-5}$	*KCTD20*	rs4711453	1	0.32	1.14	0.11	1.05	0.55	0.95	0.71
rs12698588	7	0.30	0.81	$2.15\text{x}10^{-2}$	0.70	$9.06\text{x}10^{-5}$	1.34	$5.35\text{x}10^{-2}$	$9.72\text{x}10^{-5}$	NA	rs12698588	1	0.33	1.06	0.47	0.96	0.65	0.99	0.92
rs6758063	2	0.37	1.27	$7.59\text{x}10^{-3}$	1.42	$9.10\text{x}10^{-5}$	0.69	$8.84\text{x}10^{-3}$	$1.02\text{x}10^{-4}$	*ERBB4*	rs6758063	1	0.35	0.89	0.15	0.95	0.49	1.07	0.63
rs6734290	2	0.42	0.84	$4.48\text{x}10^{-2}$	0.71	$9.95\text{x}10^{-5}$	1.45	$1.17\text{x}10^{-2}$	$1.04\text{x}10^{-4}$	*TXNDC9*	rs13013984	0.97	0.45	0.99	0.91	1.03	0.68	0.96	0.77
rs2948519	17	0.46	0.76	$2.07\text{x}10^{-3}$	0.71	$1.01\text{x}10^{-4}$	1.72	$1.42\text{x}10^{-4}$	$1.05\text{x}10^{-4}$	*KSR1*	rs2948519	1	0.47	1.00	0.95	0.97	0.69	1.01	0.96
rs11941928	4	0.43	1.19	$4.78\text{x}10^{-2}$	1.40	$1.04\text{x}10^{-4}$	0.61	$4.66\text{x}10^{-4}$	$1.04\text{x}10^{-4}$	NA	rs11133355	0.84	0.37	0.93	0.33	1.00	0.99	1.02	0.88

R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

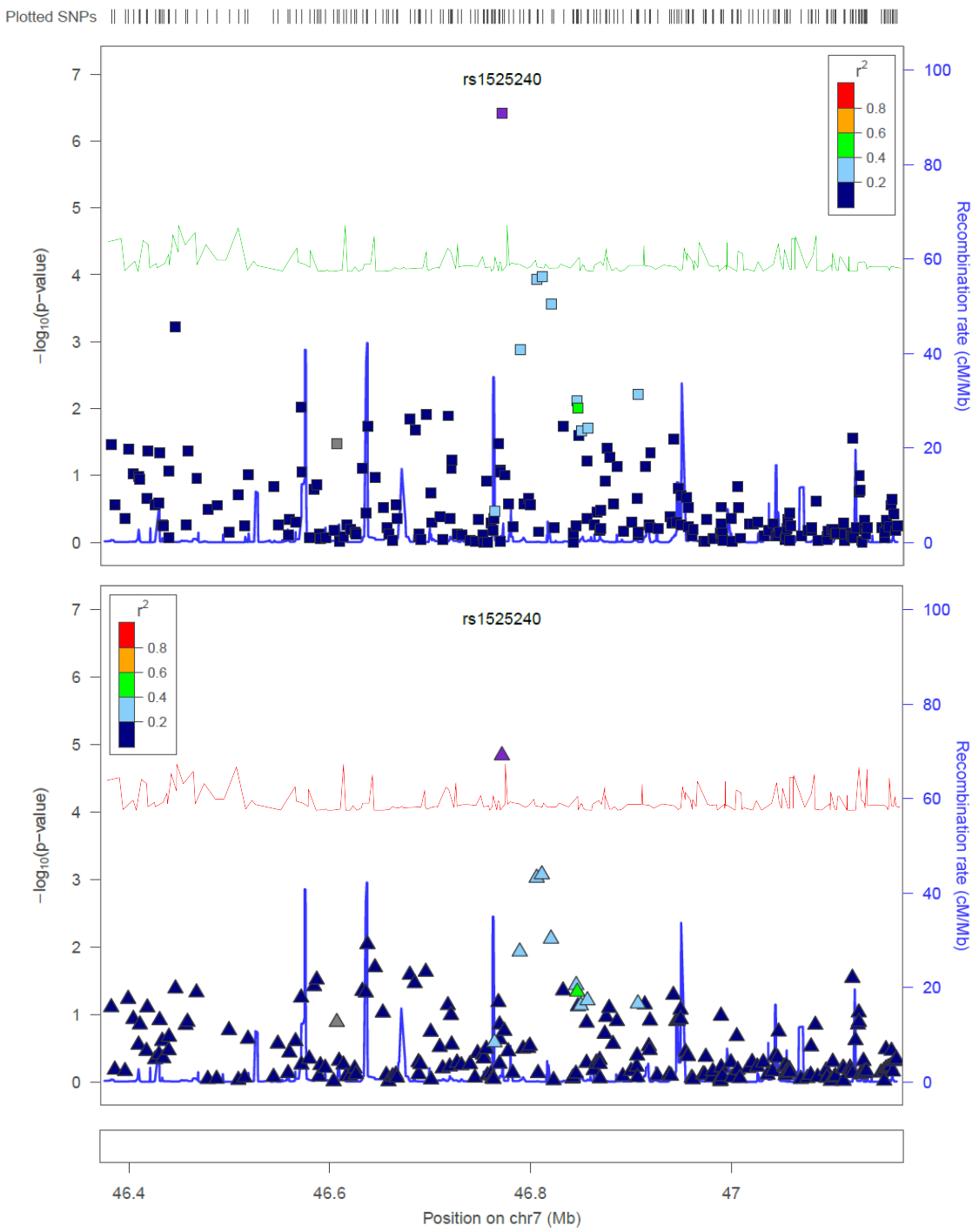


Figure S11: AGP Strict Chromosome 7, rs1525240 Paternal Over-Transmission and Maternal Effect. The top panel shows the regional plot of SNPs highlighted in the AGP Strict analysis for an imprinting effect (I_M, squares) when there is an association above the R_1 threshold (green line). The second panel shows the regional plot for maternal genetic effects (S_1, triangles) and the S_1 threshold (green line). Index SNP rs1525240 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue.

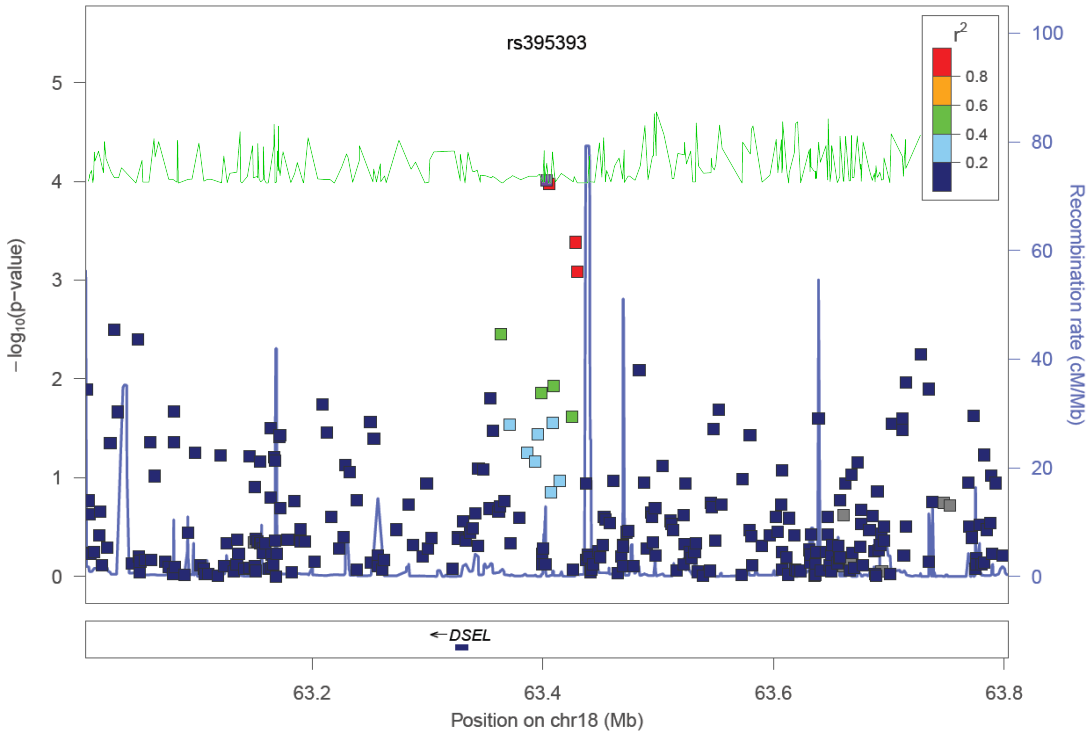


Figure S12: AGP Strict Chromosome 18, rs395393 Maternal Over-Transmission. The top panel shows the regional plot of SNPs highlighted in the AGP Strict analysis for the association (R_1, circles). When the association is above the Bayesian threshold for R_1 (green line), we then investigate the imprinting results, shown in the second panel represented by squares. Index SNP rs395393 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue.

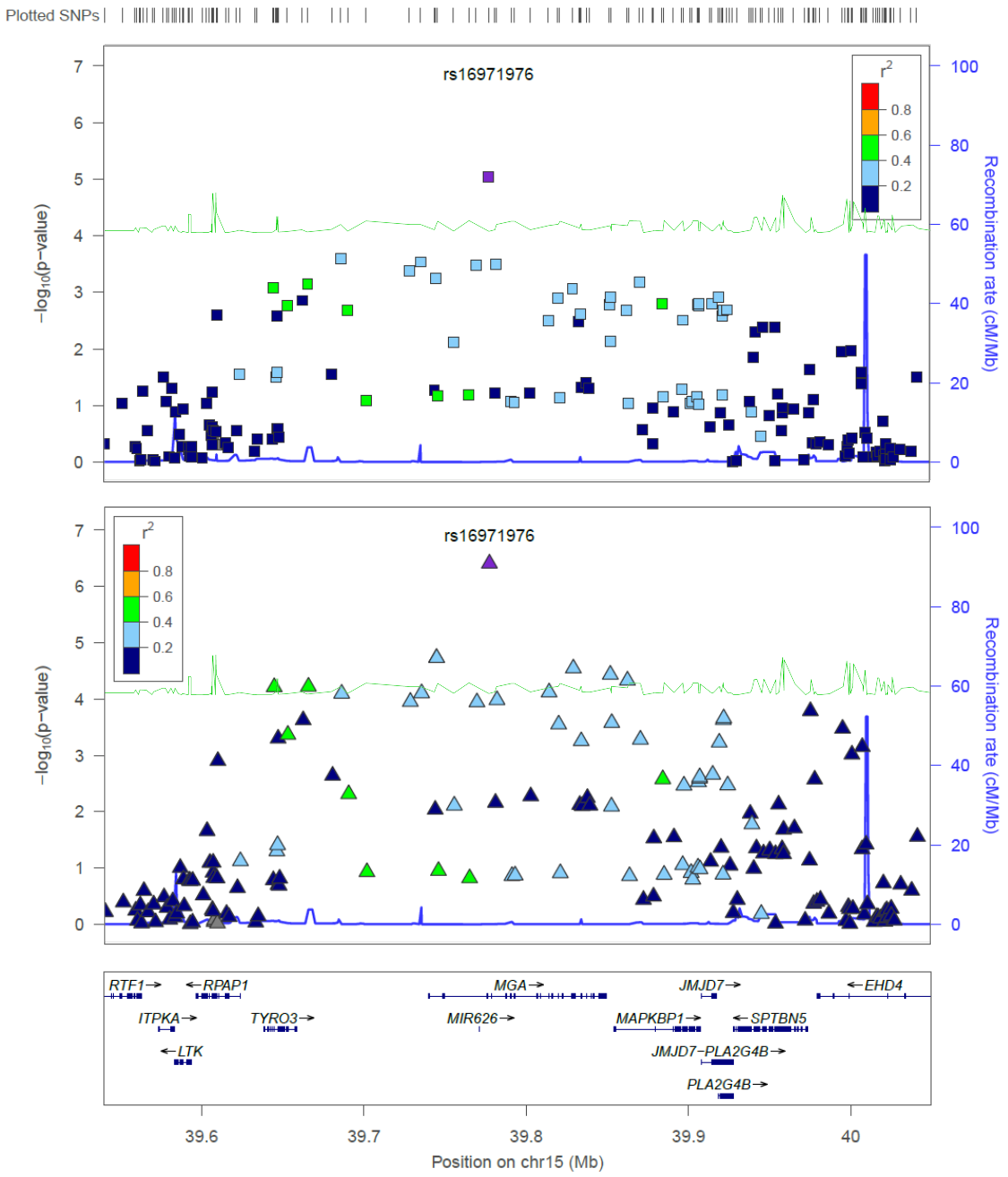
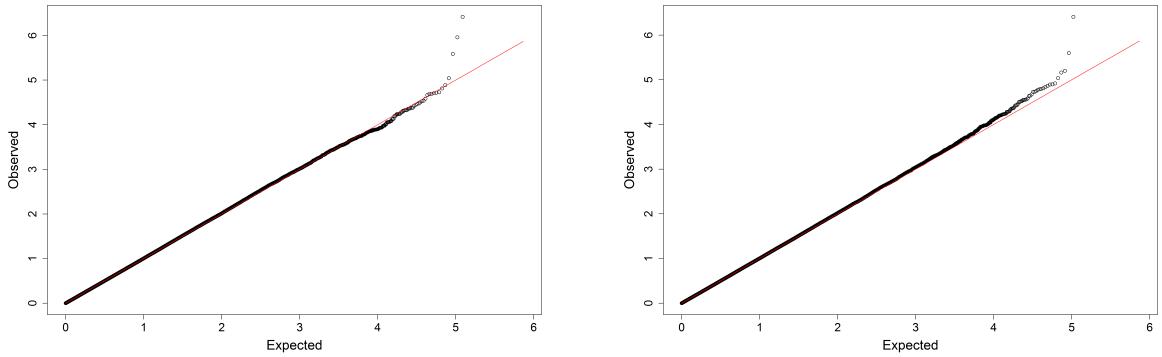


Figure S13: AGP Strict Chromosome 15, rs16971976 Paternal Over-Transmission and Maternal Effect. The top panel shows the regional plot of SNPs highlighted in the AGP Strict analysis for an imprinting effect (I_M, squares) when there is an association above the R_1 threshold (green line). The second panel shows the regional plot for maternal genetic effects (S_1, triangles) and the S_1 threshold (green line). Index SNP rs16971976 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue.



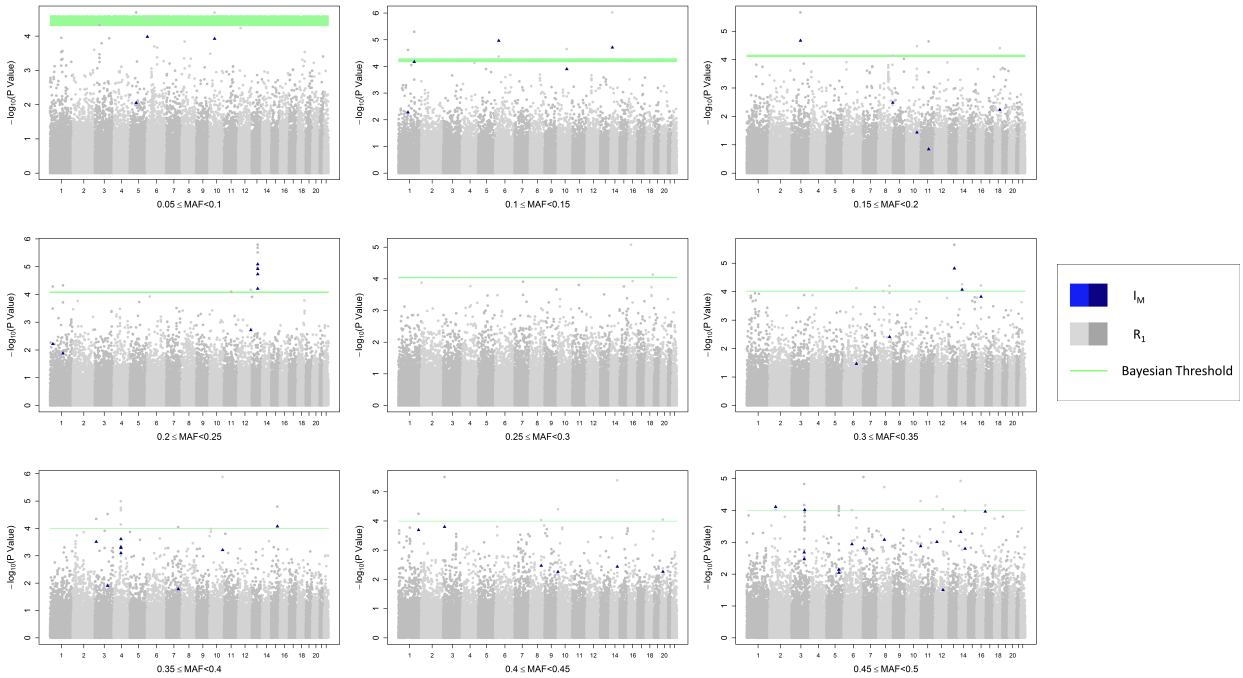
(a) I_M (b) S_1

Figure S14: QQ plots for AGP Strict dataset

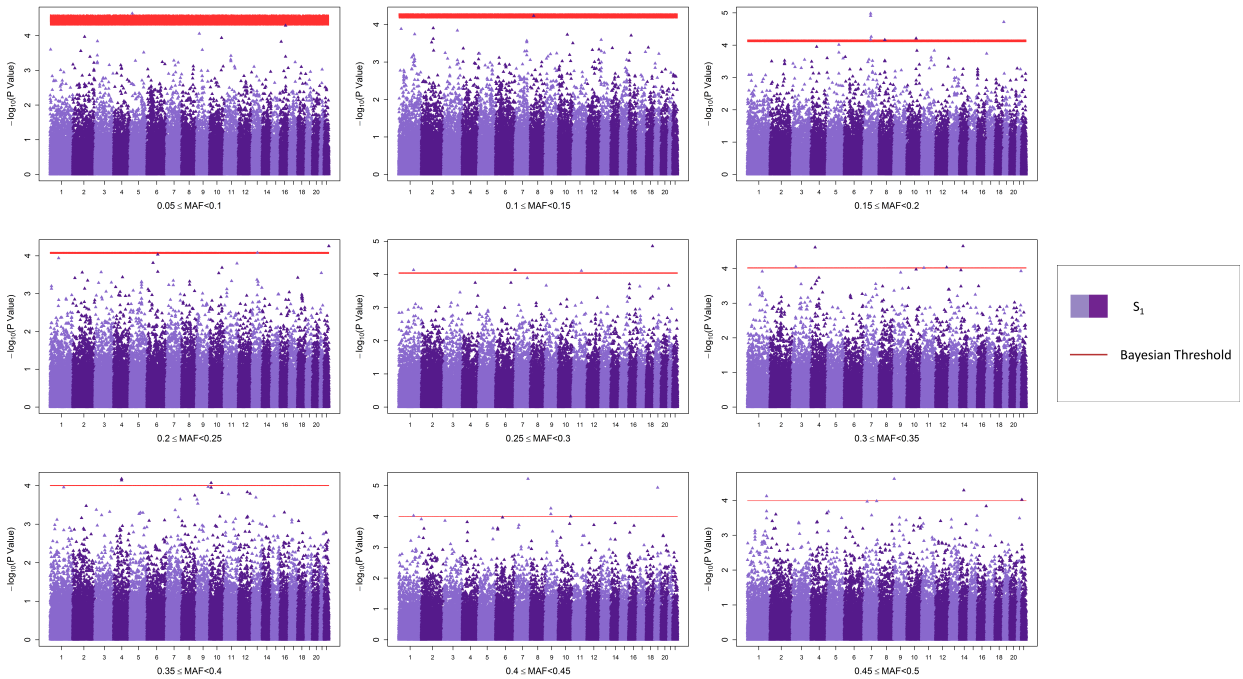
(a) I_M (b) S_1

Figure S15: Summary of AGP results, for imprinting, I_M, and maternal genetic effects, S_1, and the overlap between Strict and Spectrum datasets

SSC Spectrum Results



(a) Imprinting



(b) Maternal Genetic Effects

Figure S16: Manhattan Plots for Imprinting (Figure S16 (a)) and Maternal Genetic Effects (Figure S16 (b)) for Spectrum Phenotype in SSC dataset

Table S8: Top Imprinting Results in the SSC Spectrum dataset and the corresponding findings in the AGP Spectrum dataset

SSC Results											AGP Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	R_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs9573533	13	0.23	1.43	$3.08\text{x}10^{-6}$	1.25	$4.84\text{x}10^{-3}$	0.59	$8.17\text{x}10^{-6}$	$8.49\text{x}10^{-5}$	*TBC1D4*	rs9573533	1	0.23	1.04	0.59	0.88	0.08	0.98	0.83
rs16890706	6	0.12	0.68	$4.26\text{x}10^{-5}$	0.77	$4.31\text{x}10^{-3}$	1.86	$1.09\text{x}10^{-5}$	$5.82\text{x}10^{-5}$	*LRRC16A*	rs16890706	1	0.13	0.96	0.64	0.93	0.38	1.18	0.21
rs8013309	14	0.13	0.63	$9.47\text{x}10^{-7}$	0.77	$3.73\text{x}10^{-3}$	1.81	$1.95\text{x}10^{-5}$	$6.16\text{x}10^{-5}$	NA	rs8013309	1	0.13	1.07	0.45	0.95	0.59	0.97	0.82
rs7651342	3	0.16	1.51	$2.17\text{x}10^{-6}$	1.37	$5.08\text{x}10^{-4}$	0.57	$2.14\text{x}10^{-5}$	$7.11\text{x}10^{-5}$	*RP11-260O18.1*	rs7651342	1	0.14	0.96	0.60	0.97	0.77	1.15	0.29
rs16860429	1	0.12	1.59	$5.01\text{x}10^{-6}$	1.46	$1.80\text{x}10^{-4}$	0.56	$6.75\text{x}10^{-5}$	$6.75\text{x}10^{-5}$	NA	rs16860429	1	0.11	1.22	0.04	1.22	0.04	0.75	0.05
rs165052	2	0.46	1.32	$9.57\text{x}10^{-5}$	1.18	$2.05\text{x}10^{-2}$	0.63	$7.75\text{x}10^{-5}$	$1.02\text{x}10^{-4}$	*EML6*	rs165052	1	0.46	1.05	0.49	1.02	0.74	0.98	0.88
rs2136980	15	0.40	0.74	$1.61\text{x}10^{-5}$	0.83	$7.76\text{x}10^{-3}$	1.56	$8.42\text{x}10^{-5}$	$1.00\text{x}10^{-4}$	NA	rs2136980	1	0.40	1.04	0.58	1.01	0.84	1.08	0.50
rs17124893	14	0.33	1.34	$5.48\text{x}10^{-5}$	1.36	$2.25\text{x}10^{-5}$	0.64	$8.48\text{x}10^{-5}$	$9.64\text{x}10^{-5}$	*NID2*	rs17124893	1	0.32	0.98	0.77	1.03	0.65	0.98	0.84
rs9647337	3	0.45	1.31	$1.01\text{x}10^{-4}$	1.19	$1.37\text{x}10^{-2}$	0.64	$9.68\text{x}10^{-5}$	$1.02\text{x}10^{-4}$	*PIK3CB*	rs11720178	1	0.46	0.96	0.52	1.02	0.73	0.92	0.46

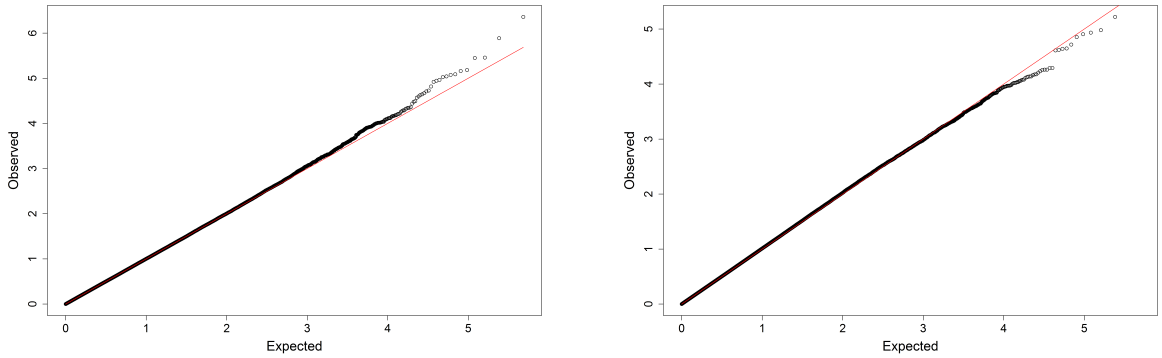
R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

Table S9: Maternal Genetic Effects Results in the SSC Spectrum dataset and the corresponding findings in the AGP Spectrum dataset

SSC Results											AGP Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	S_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs6967953	7	0.41	1.19	$1.67\text{x}10^{-2}$	1.38	$6.01\text{x}10^{-6}$	0.61	$3.31\text{x}10^{-5}$	$1.01\text{x}10^{-4}$	*CHRM2*	rs6967953	1	0.41	0.97	0.65	0.92	0.20	1.13	0.26
rs10499761	7	0.18	1.36	$2.80\text{x}10^{-4}$	1.44	$1.05\text{x}10^{-5}$	0.61	$7.60\text{x}10^{-5}$	$7.51\text{x}10^{-5}$	NA	rs10499761	1	0.17	1.07	0.43	1.08	0.31	0.94	0.60
rs10415705	19	0.42	0.89	$1.15\text{x}10^{-1}$	0.73	$1.16\text{x}10^{-5}$	1.37	$5.99\text{x}10^{-3}$	$1.01\text{x}10^{-4}$	NA	rs10415705	1	0.42	1.02	0.81	1.02	0.82	1.00	0.99
rs9953010	18	0.28	1.15	$6.66\text{x}10^{-2}$	1.38	$1.40\text{x}10^{-5}$	0.66	$4.86\text{x}10^{-4}$	$9.18\text{x}10^{-5}$	NA	rs9953010	1	0.29	0.98	0.77	1.01	0.88	1.04	0.75
rs10424718	19	0.16	0.73	$1.98\text{x}10^{-4}$	0.70	$1.92\text{x}10^{-5}$	1.55	$7.98\text{x}10^{-4}$	$7.02\text{x}10^{-5}$	*CELF5*	rs10424718	1	0.15	1.05	0.56	0.96	0.68	1.05	0.72
rs17124893	14	0.33	1.34	$5.48\text{x}10^{-5}$	1.36	$2.25\text{x}10^{-5}$	0.64	$8.48\text{x}10^{-5}$	$9.64\text{x}10^{-5}$	*NID2*	rs17124893	1	0.32	0.98	0.77	1.03	0.65	0.98	0.84
rs10042810	5	0.07	1.16	$2.56\text{x}10^{-1}$	1.67	$2.29\text{x}10^{-5}$	0.63	$1.11\text{x}10^{-2}$	$3.34\text{x}10^{-5}$	NA	rs10042810	1	0.06	0.83	0.10	0.80	0.05	1.24	0.20
rs1339359	9	0.50	1.25	$1.31\text{x}10^{-3}$	1.35	$2.39\text{x}10^{-5}$	0.72	$4.51\text{x}10^{-3}$	$1.02\text{x}10^{-4}$	NA	rs1339359	1	0.50	0.99	0.93	1.04	0.53	0.97	0.81
rs4861106	4	0.32	0.85	$2.66\text{x}10^{-2}$	0.74	$2.44\text{x}10^{-5}$	1.39	$4.08\text{x}10^{-3}$	$9.56\text{x}10^{-5}$	NA	rs4861106	1	0.30	1.10	0.18	1.03	0.70	0.86	0.19
rs8016570	14	0.46	1.17	$2.94\text{x}10^{-2}$	1.34	$5.11\text{x}10^{-5}$	0.77	$2.81\text{x}10^{-2}$	$1.02\text{x}10^{-4}$	*DAAM1*	rs8016570	1	0.46	1.12	0.11	1.06	0.38	0.83	0.10
rs610529	9	0.44	1.21	$6.74\text{x}10^{-3}$	1.32	$5.46\text{x}10^{-5}$	0.68	$6.49\text{x}10^{-4}$	$1.01\text{x}10^{-4}$	*ALDH1A1*	rs610529	1	0.44	1.14	0.05	1.01	0.93	0.93	0.48
rs4719103	7	0.16	1.23	$2.08\text{x}10^{-2}$	1.41	$5.48\text{x}10^{-5}$	0.61	$1.79\text{x}10^{-4}$	$6.98\text{x}10^{-5}$	*WBSCR17*	rs4719103	1	0.15	1.02	0.84	0.96	0.63	0.93	0.60
rs5770820	22	0.21	1.25	$5.74\text{x}10^{-3}$	1.38	$5.54\text{x}10^{-5}$	0.64	$3.82\text{x}10^{-4}$	$8.16\text{x}10^{-5}$	*SHANK3*	rs5770820	1	0.21	0.83	0.02	0.98	0.82	1.24	0.08
rs12676446	8	0.12	1.20	$7.67\text{x}10^{-2}$	1.47	$5.84\text{x}10^{-5}$	0.77	$7.28\text{x}10^{-2}$	$5.88\text{x}10^{-5}$	*PSD3*	rs12676446	1	0.11	0.98	0.86	1.03	0.74	0.96	0.78
rs11201909	10	0.16	0.88	$1.11\text{x}10^{-1}$	0.71	$6.18\text{x}10^{-5}$	1.30	$4.49\text{x}10^{-2}$	$7.14\text{x}10^{-5}$	*GRID1*	rs11201909	1	0.15	1.04	0.62	0.98	0.80	0.94	0.62
rs10021524	4	0.39	1.18	$2.45\text{x}10^{-2}$	1.33	$6.63\text{x}10^{-5}$	0.74	$9.21\text{x}10^{-3}$	$9.99\text{x}10^{-5}$	*CCSER1*	rs10021524	1	0.39	1.04	0.54	1.05	0.51	0.90	0.34
rs12549180	8	0.19	1.33	$6.92\text{x}10^{-4}$	1.40	$6.87\text{x}10^{-5}$	0.69	$2.53\text{x}10^{-3}$	$7.74\text{x}10^{-5}$	NA	rs12549180	1	0.18	1.07	0.39	1.00	0.95	0.89	0.36
rs1000104	6	0.29	1.20	$1.55\text{x}10^{-2}$	1.34	$7.27\text{x}10^{-5}$	0.72	$4.15\text{x}10^{-3}$	$9.24\text{x}10^{-5}$	NA	rs1000104	1	0.27	0.94	0.43	0.96	0.60	1.12	0.32
rs7515001	1	0.29	0.79	$1.41\text{x}10^{-3}$	0.74	$7.34\text{x}10^{-5}$	1.46	$1.42\text{x}10^{-3}$	$9.22\text{x}10^{-5}$	*GM2AP2*	rs7515001	1	0.28	1.01	0.93	1.03	0.69	0.95	0.67
rs1995873	1	0.47	0.80	$1.86\text{x}10^{-3}$	0.76	$7.51\text{x}10^{-5}$	1.57	$9.66\text{x}10^{-5}$	$1.02\text{x}10^{-4}$	*LINC00210*	rs1995873	1	0.48	1.13	0.07	1.06	0.35	0.88	0.26
rs2173281	11	0.28	1.23	$5.99\text{x}10^{-3}$	1.34	$7.72\text{x}10^{-5}$	0.65	$1.80\text{x}10^{-4}$	$9.19\text{x}10^{-5}$	NA	rs2173281	1	0.30	0.97	0.68	0.98	0.73	1.05	0.65
rs11256031	10	0.36	1.33	$1.04\text{x}10^{-4}$	1.33	$8.45\text{x}10^{-5}$	0.66	$4.13\text{x}10^{-4}$	$9.83\text{x}10^{-5}$	NA	rs11256031	1	0.35	0.98	0.78	1.01	0.90	1.02	0.83
rs4973800	3	0.34	0.82	$7.04\text{x}10^{-3}$	0.75	$8.81\text{x}10^{-5}$	1.58	$9.62\text{x}10^{-5}$	$9.68\text{x}10^{-5}$	*LRRC3B*	rs4973800	1	0.34	1.12	0.10	1.06	0.41	0.86	0.15
rs933296	12	0.31	0.87	$4.68\text{x}10^{-2}$	0.75	$9.21\text{x}10^{-5}$	1.30	$2.79\text{x}10^{-2}$	$9.48\text{x}10^{-5}$	*MYL2*	rs933296	1	0.32	1.03	0.72	1.03	0.69	0.90	0.37
rs2207189	1	0.40	1.20	$1.08\text{x}10^{-2}$	1.33	$9.45\text{x}10^{-5}$	0.71	$3.10\text{x}10^{-3}$	$1.00\text{x}10^{-4}$	*RNU6-290P*	rs2207189	1	0.40	0.90	0.14	0.94	0.36	1.12	0.31
rs11704083	22	0.49	0.87	$5.59\text{x}10^{-2}$	0.76	$9.52\text{x}10^{-5}$	1.40	$3.33\text{x}10^{-3}$	$1.02\text{x}10^{-4}$	*GNB1L*	rs11704083	1	0.48	1.09	0.20	1.00	0.95	0.92	0.46
rs1932543	10	0.43	1.19	$1.59\text{x}10^{-2}$	1.32	$9.94\text{x}10^{-5}$	0.71	$3.24\text{x}10^{-3}$	$1.01\text{x}10^{-4}$	NA	rs1932543	1	0.41	0.90	0.14	0.87	0.05	1.29	0.02

R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

Figure S17 gives the QQ plots for I_M and S_1 in the SSC Spectrum dataset.



(a) I_M (b) S_1

Figure S17: QQ plots for SSC Spectrum dataset

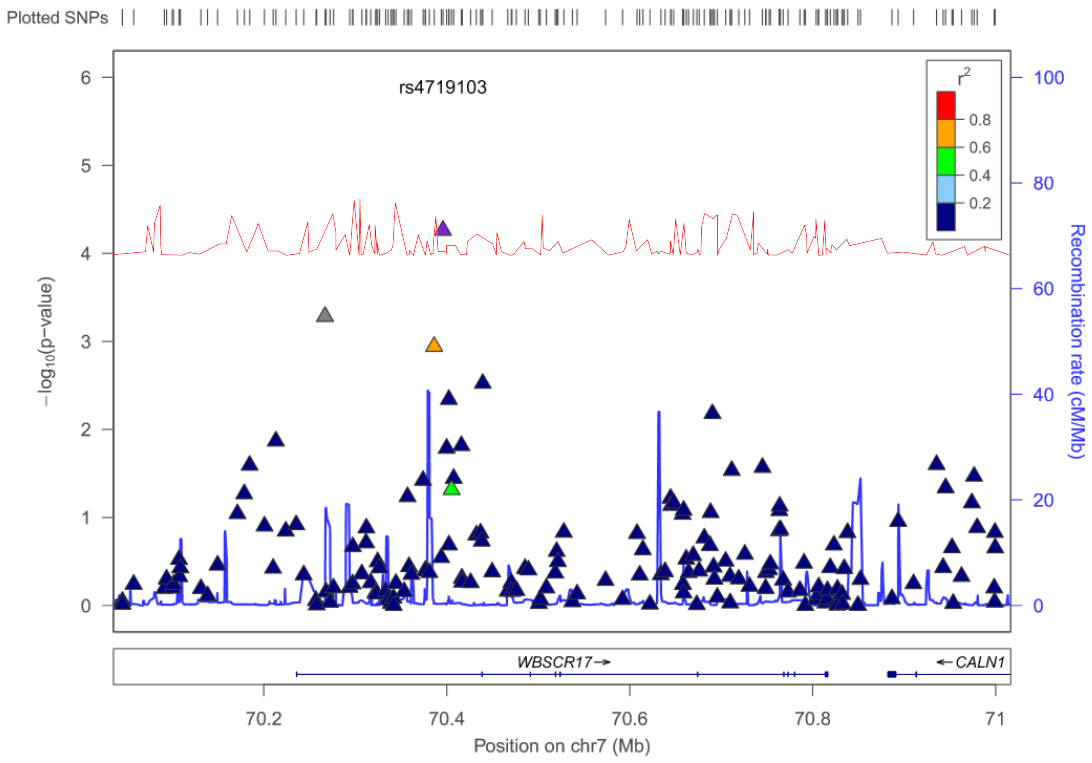


Figure S18: SSC Spectrum Chromosome 7, rs4719103 Maternal Genetic Effect. Regional plot of SNPs highlighted in the SSC Spectrum analysis for maternal genetic effects (S_1, triangles). Index SNP rs4719103 is shown in purple. Markers in linkage disequilibrium with the index SNP are shown and based on 1000 genomes CEU. Recombination rate plotted in blue. The red line represents the Bayesian threshold for S_1.

SSC Strict Results

There were three noteworthy imprinting results (one of which overlaps with the SSC Spectrum results) and there were twenty-four independent loci with a maternal genetic effect above the S_1 threshold (six of which overlap with the SSC Strict results), see the Manhattan plots (Figure S19) and Tables S10 and S11. Figure S21 gives an the overlap of findings that where above the threshold in both the SSC Strict and SSC Spectrum. Note that many findings where above the threshold in one of the phenotypes and close but not above the threshold in the other phenotype and hence. were not noted as noteworthy findings. Figure S20 gives the QQ plots for I_M and S_1 in the SSC Strict dataset.

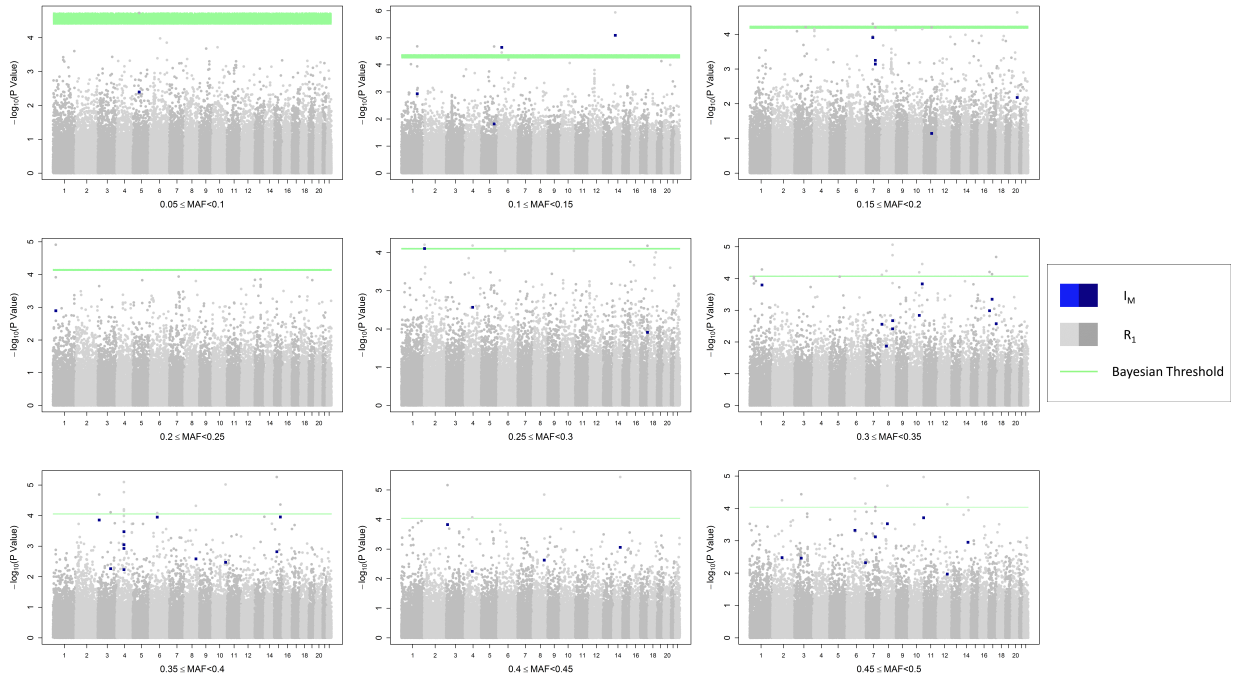
Imprinting Results

Our strongest associations showed evidence for maternal over-transmission on chromosome 14q13 within 10.7kb of the *NFKBIA* gene (rs8013309, $I_M = 2$, Wald p-value = $8.08\text{x}10^{-6}$). This area was previously linked with intellectual and developmental disabilities in a CNV study [26]. One of our top hits for maternal over-transmission on chromosome 6p is located in the *LRRC16A* gene (near the *HLA* region) (rs16890706, $I_M = 1.94$, Wald p-value = $2.25\text{x}10^{-5}$), which was previously implicated in language deficits in [27]. Another noteworthy maternal over-transmission result was found on chromosome 2 in the *DCDC2C* gene (rs357977, $I_M = 1.707$, Wald p-value = $7.86\text{x}10^{-5}$), which was previously implicated in low IQ in autism and other neurodevelopmental disorders [28].

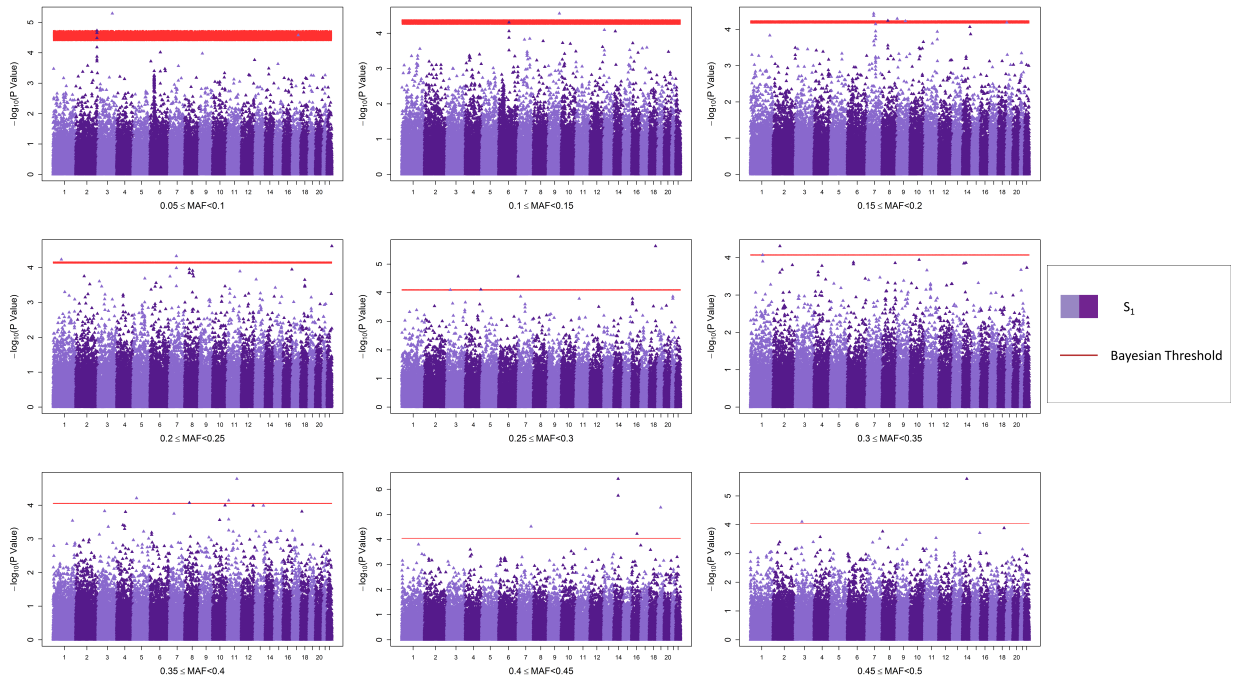
Maternal Genetic Results

We found evidence for a maternal genetic effect on chromosome 14q in the *DAAM1* gene (rs1253005, $S_1 = 1.51$, Wald p-value = 3.84^{-7}). This area was previously implicated in a CNV study for intellectual and developmental disabilities [26]. One of our top hits for maternal genetic effects

is on chromosome 22 in the *SHANK3* gene (rs5770820, $S_1 = 1.46$, Wald p-value = $2.45\text{x}10^{-5}$), and disruptions in the *SHANK3* gene have been associated with autistic traits and in particular, these disruptions are responsible for the development of Phelan–McDermid syndrome and other non-syndromic ASDs [29]. A noteworthy protective maternal genetic effect result was identified on chromosome 16q21 in the *CDH8* gene (rs11075447, $S_1 = 0.72$, Wald p-value = $5.94\text{x}10^{-5}$), with evidence of disruptions in *CDH8* in two families being previously linked to autism and learning disability [30].



(a) Imprinting



(b) Maternal Genetic Effects

Figure S19: Manhattan Plots for Imprinting (Figure S19 (a)) and Maternal Genetic Effects (Figure S19 (b)) for Strict Phenotype in SSC dataset

Table S10: Top Imprinting Results in the SSC Strict dataset and the corresponding findings in the AGP Strict dataset

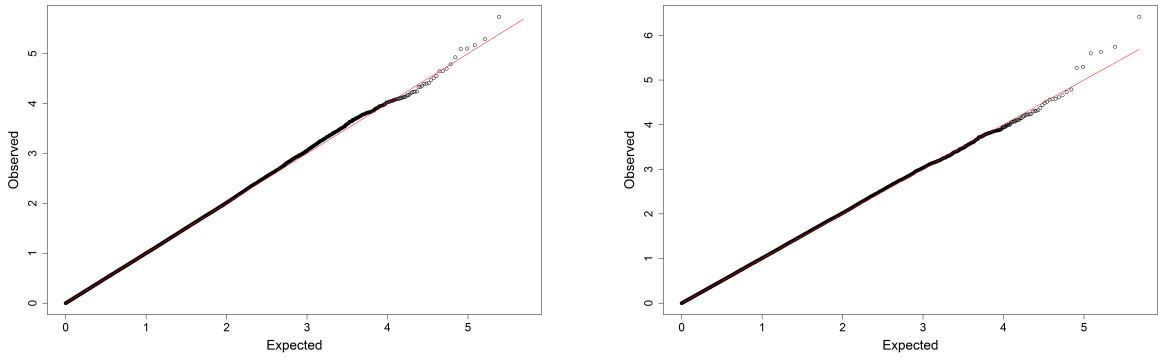
SSC Results											AGP Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	R_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs8013309	14	0.13	0.60	$1.15\text{x}10^{-6}$	0.72	$7.79\text{x}10^{-4}$	2.01	$8.08\text{x}10^{-6}$	$5.01\text{x}10^{-5}$	NA	rs8013309	1	0.13	1.04	0.72	0.90	0.39	1.11	0.55
rs16890706	6	0.12	0.65	$3.48\text{x}10^{-5}$	0.74	$3.52\text{x}10^{-3}$	1.94	$2.25\text{x}10^{-5}$	$4.87\text{x}10^{-5}$	*LRRC16A*	rs16890706	1	0.13	0.87	0.19	0.86	0.18	1.30	0.11
rs357977	2	0.28	0.71	$6.26\text{x}10^{-5}$	0.88	$1.32\text{x}10^{-1}$	1.71	$7.86\text{x}10^{-5}$	$8.02\text{x}10^{-5}$	*DCDC2C*	rs357977	1	0.28	0.86	0.09	0.95	0.57	1.18	0.25

R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.

Table S11: Maternal Genetic Effects Results in the SSC Strict dataset and the corresponding findings in the AGP Strict dataset

SSC Results											AGP Results								
SNP	Chr	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M	S_1 Threshold	Gene	SNP	R^2	MAF	R_1	PV R_1	S_1	PV S_1	I_M	PV I_M
rs1253005	14	0.43	1.30	$1.23\text{x}10^{-3}$	1.51	$3.84\text{x}10^{-7}$	0.62	$3.18\text{x}10^{-4}$	$9.05\text{x}10^{-5}$	*DAAM1*	rs1253005	1	0.43	1.04	0.64	0.90	0.22	1.00	0.99
rs9953010	18	0.27	1.23	$1.76\text{x}10^{-2}$	1.48	$2.34\text{x}10^{-6}$	0.59	$9.86\text{x}10^{-5}$	$7.96\text{x}10^{-5}$	NA	rs9953010	1	0.28	0.91	0.30	1.07	0.49	1.01	0.93
rs6440688	3	0.09	0.77	$1.66\text{x}10^{-2}$	0.58	$5.09\text{x}10^{-6}$	1.70	$2.40\text{x}10^{-3}$	$3.86\text{x}10^{-5}$	*SELT*	rs6440688	1	0.09	0.86	0.27	0.86	0.26	1.17	0.43
rs10415705	19	0.42	0.88	$1.09\text{x}10^{-1}$	0.70	$5.32\text{x}10^{-6}$	1.43	$5.13\text{x}10^{-3}$	$9.02\text{x}10^{-5}$	NA	rs10415705	1	0.42	1.01	0.94	1.04	0.64	0.98	0.90
rs7939358	11	0.37	0.76	$4.21\text{x}10^{-4}$	0.71	$1.63\text{x}10^{-5}$	1.62	$1.04\text{x}10^{-4}$	$8.76\text{x}10^{-5}$	NA	rs7939358	1	0.36	1.09	0.33	0.95	0.61	1.11	0.46
rs12052787	2	0.07	1.57	$1.59\text{x}10^{-3}$	1.82	$1.85\text{x}10^{-5}$	0.53	$9.46\text{x}10^{-4}$	$2.64\text{x}10^{-5}$	*UGT1A*	rs12052787	1	0.06	0.86	0.32	1.06	0.69	1.14	0.56
rs5770820	22	0.21	1.25	$1.45\text{x}10^{-2}$	1.46	$2.45\text{x}10^{-5}$	0.60	$2.50\text{x}10^{-4}$	$6.99\text{x}10^{-5}$	*SHANK3*	rs5770820	1	0.21	0.76	0.01	0.97	0.78	1.36	0.05
rs1009962	17	0.09	0.69	$1.10\text{x}10^{-3}$	0.60	$2.63\text{x}10^{-5}$	2.05	$4.70\text{x}10^{-5}$	$3.55\text{x}10^{-5}$	*TBX4*	rs1009962	1	0.09	0.87	0.29	0.93	0.59	1.26	0.23
rs1000104	6	0.29	1.23	$1.33\text{x}10^{-2}$	1.41	$2.67\text{x}10^{-5}$	0.66	$1.74\text{x}10^{-3}$	$8.08\text{x}10^{-5}$	NA	rs1000104	1	0.28	0.98	0.86	1.05	0.57	1.03	0.86
rs10306143	9	0.13	0.87	$1.70\text{x}10^{-1}$	0.64	$2.75\text{x}10^{-5}$	1.81	$1.23\text{x}10^{-4}$	$4.96\text{x}10^{-5}$	*PTGS1*	rs10306143	1	0.13	0.99	0.92	0.98	0.85	1.04	0.82
rs6967953	7	0.41	1.22	$1.53\text{x}10^{-2}$	1.39	$3.05\text{x}10^{-5}$	0.65	$8.86\text{x}10^{-4}$	$8.99\text{x}10^{-5}$	*CHRM2*	rs6967953	1	0.41	0.93	0.43	0.85	0.06	1.28	0.08
rs10499761	7	0.18	1.43	$1.14\text{x}10^{-4}$	1.47	$3.64\text{x}10^{-5}$	0.57	$4.38\text{x}10^{-5}$	$6.42\text{x}10^{-5}$	*LOC105375288*	rs10499761	1	0.18	0.98	0.84	1.05	0.62	0.99	0.93
rs2539668	2	0.31	1.26	$5.68\text{x}10^{-3}$	1.40	$4.91\text{x}10^{-5}$	0.64	$8.89\text{x}10^{-4}$	$8.32\text{x}10^{-5}$	NA	rs2539668	1	0.31	1.09	0.33	1.15	0.12	0.84	0.21
rs7046834	9	0.16	0.86	$1.31\text{x}10^{-1}$	0.66	$5.08\text{x}10^{-5}$	1.75	$3.13\text{x}10^{-4}$	$5.85\text{x}10^{-5}$	NA	rs7046834	1	0.14	0.99	0.95	0.96	0.73	1.06	0.71
rs12549180	8	0.19	1.32	$3.34\text{x}10^{-3}$	1.45	$5.74\text{x}10^{-5}$	0.66	$2.63\text{x}10^{-3}$	$6.66\text{x}10^{-5}$	NA	rs12549180	1	0.19	0.97	0.77	0.86	0.13	1.04	0.80
rs7534535	1	0.25	1.16	$8.15\text{x}10^{-2}$	1.40	$5.88\text{x}10^{-5}$	0.69	$4.70\text{x}10^{-3}$	$7.62\text{x}10^{-5}$	*ADGRL2*	rs7534535	1	0.25	0.92	0.41	1.05	0.62	1.02	0.92
rs10988794	9	0.17	1.11	$2.78\text{x}10^{-1}$	1.46	$5.90\text{x}10^{-5}$	0.71	$1.99\text{x}10^{-2}$	$6.21\text{x}10^{-5}$	NA	rs10988794	1	0.17	1.01	0.89	1.03	0.78	0.89	0.44
rs11075447	16	0.43	0.81	$9.43\text{x}10^{-3}$	1.00	$5.94\text{x}10^{-5}$	1.57	$5.05\text{x}10^{-4}$	$9.05\text{x}10^{-5}$	*CDH8*	rs11075447	1	0.43	1.03	0.78	0.95	0.56	1.02	0.92
rs7719969	5	0.36	0.84	$2.44\text{x}10^{-2}$	0.72	$6.14\text{x}10^{-5}$	1.39	$1.11\text{x}10^{-2}$	$8.71\text{x}10^{-5}$	*ADAMTS12*	rs7719969	1	0.35	1.04	0.69	1.06	0.50	0.97	0.81
rs10840106	11	0.39	1.24	$7.34\text{x}10^{-3}$	1.37	$7.13\text{x}10^{-5}$	0.64	$4.55\text{x}10^{-4}$	$8.88\text{x}10^{-5}$	*RPL27A*	rs10840106	1	0.39	0.89	0.18	0.91	0.29	1.22	0.16
rs6851029	4	0.26	1.33	$8.65\text{x}10^{-4}$	1.39	$7.71\text{x}10^{-5}$	0.65	$9.26\text{x}10^{-4}$	$7.82\text{x}10^{-5}$	NA	NA	0							
rs7612797	3	0.48	1.14	$8.36\text{x}10^{-2}$	1.36	$7.82\text{x}10^{-5}$	0.68	$1.99\text{x}10^{-3}$	$9.13\text{x}10^{-5}$	*FHIT*	rs7612797	1	0.49	0.99	0.93	1.13	0.15	0.89	0.39
rs4733037	8	0.36	1.21	$1.73\text{x}10^{-2}$	1.36	$8.46\text{x}10^{-5}$	0.68	$2.38\text{x}10^{-3}$	$8.70\text{x}10^{-5}$	*STMN4*	rs4733037	1	0.34	1.03	0.78	1.02	0.85	0.97	0.84
rs7530962	1	0.35	0.76	$6.20\text{x}10^{-4}$	0.73	$8.48\text{x}10^{-5}$	1.57	$3.24\text{x}10^{-4}$	$8.63\text{x}10^{-5}$	NA	rs7530962	1	0.34	1.07	0.44	1.05	0.59	0.92	0.56

R_1 denotes the relative risk for the offspring having one copy of the variant allele, S_1 denotes the relative risk for the mother having one copy of the variant allele, I_M denotes the relative risk for a maternal over-transmission of the allele, and PV denotes p-value.



(a) I_M **(b)** S_1

Figure S20: QQ plots for SSC Strict dataset

(a) I_M **(b)** S_1

Figure S21: Summary of SSC results for imprinting, I_M, and maternal genetic effects, S_1, and the overlap between Strict and Spectrum datasets

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